The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 110, NO. 26 — COPYRIGHT, 1938, BY AMERICAN MEDICAL ASSOCIATION CHICAGO, ILLINOIS — JUNE 25, 1938

SUPPOSED ROLE OF THE ADRENALS IN HYPERTENSION

AN EXPERIMENTAL INVESTIGATION

J. M. ROGOFF, M.D., D.Sc.
AND
EMANUEL MARCUS, PH.D.
CHICAGO

Our experiments constitute part of an investigation on the alleged relation of the adrenal medulla to certain diseases, particularly diabetes mellitus and hypertension. The supposition of such a relation is a basis for the clinical practice of surgical intervention at the adrenals or roentgen irradiation of the adrenal region as a therapeutic measure. Therefore it is important to determine if possible whether this alleged relationship can be supported by unequivocal experimental evidence.

The prevailing concept that increased epinephrine secretion from the adrenal glands has an important role in the etiology and the pathology of hypertension rests largely on the experimental basis for the theory of an "emergency" function of the adrenals. In a discussion of their experiments on epinephrine secretion during emotional excitement, on which the well known emergency theory rests, Cannon and de la Paz [1] stated:

> Injected epinephrine is capable of inducing an atheromatous condition of the arterial wall in rabbits, especially in elderly individuals, and is also capable of evoking hyperglycemia with glycosuria. As Ascher has shown, by prolonged stimulation of the splanchnic nerves, prolonged secretion of epinephrine with maintained high blood pressure can be produced. In the light of the results here reported the temptation is strong to suggest that some phases of these pathologic states are associated with the strenuous and exciting character of modern life acting through the adrenal glands.

They [2] further suggested the possibility that "some of the adrenal secretion set free by nervous stimulation returns to the glands in the blood stream, and, within limits, stimulates them to further activity" and in this manner produces an "autogenous continuance of adrenal secretion."

If this occurs, it is conceivable that it might lead to continued liberation of epinephrine in sufficient amounts to cause a persistent elevation of blood pressure. However, it seems paradoxic that a physiologic mechanism presumably evolved to serve the organism in emergencies should at the same time constitute a serious potential menace. For, if the aforementioned suggestions, made by Cannon and de la Paz, are carried to a logical conclusion, emotional excitement should initiate a cycle of continuous secretion of epinephrine and inevitably lead to development of diabetes and hypertension. Unless it is assumed that the adrenals are soon fatigued, the question arises how such a cycle would be terminated. It has been demonstrated that the peripheral mechanism for secretion of epinephrine is not readily fatigued.[3] Repeated splanchnic stimulation at short intervals over many hours was performed without causing adrenal fatigue. When the experiment was terminated the adrenal was still capable of responding further to splanchnic stimulation. Not only was the output of epinephrine increased by the repeated stimulation but its production by the gland was augmented.

The experiments of Dragstedt, Prohaska and Harms [4] on experimental hypertension demonstrate that continuous intravenous injection of epinephrine in dogs in amounts corresponding to from five to fifteen times the average normal quantity secreted from the adrenals, as determined by Stewart and Rogoff,[5] cannot be continued for longer than a few days without serious or fatal consequence. Similar results, occurring within a few hours, were observed by us when doses three or more times as large as those employed by Dragstedt and his co-workers were administered. Our experiments support the conclusion, drawn by Dragstedt, Prohaska and Harms, that "it seems very probable that a degree of hyperadrenalinemia sufficient to produce hypertension would soon cause the death of the individual from other systemic effects of the hormone" and that "for this reason it does not seem probable that persistent hypertension in man will be found to be due to hyperadrenalinemia."

If epinephrine secretion is in any way related to production of hypertension, it would seem probable that other factors might render the circulatory or vasomotor apparatus hypersensitive to epinephrine, which could then induce hypertension in the amounts ordinarily secreted. We are attempting to study this possibility in another investigation. The present report includes

From the Physiological Laboratory, University of Chicago.

A preliminary report has been published (Rogoff, J. M.; Nixon, E. Nola; Stewart, George N., and Marcus, Emanuel: Proc. Soc. Exper. Biol. & Med. **37**: 715 [Jan.] 1938).

Aided by a grant from the Rosenwald Family Association and by the G. N. Stewart Memorial Fund, contributed by the Louis D. Beaumont Trust, N. L. Dauby, Richard H. Kohn, Mrs. Frances W. Lang and Howard E. Wise.

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2. Cannon, W. B., and de la Paz, D.: Emotional Stimulation of Adrenal Secretion, Am. J. Physiol. **28**: 64, 1911.
3. Stewart, G. N., and Rogoff, J. M.: The Liberation of Epinephrine from the Adrenal Glands by Stimulation of the Splanchnic Nerves and by Massage, J. Pharmacol. & Exper. Therap. **8**: 205 (May) 1916; The Spontaneous Liberation of Epinephrine from the Adrenals, ibid. **8**: 479 (Sept.) 1916.
4. Dragstedt, L. R.; Prohaska, J. V., and Harms, H. P.: The Effect of the Continuous Intravenous Injection of Epinephrine on the Blood Pressure, Am. J. Physiol. **119**: 298 (June) 1937; Ann. Surg. **106**: 857 (Nov.) 1937.
5. Stewart, G. N., and Rogoff, J. M.: The Average Epinephrine Output in Cats and Dogs, Am. J. Physiol. **66**: 235 (Feb.) 1923.

quantitative studies on the output of epinephrine from the adrenals and on its disappearance from the systemic circulation after intravenous injection of various amounts.

QUANTITATIVE EXPERIMENTS ON THE RATE OF SECRETION OF EPINEPHRINE AFTER INTRAVENOUS ADMINISTRATION OF EPINEPHRINE

We made quantitative measurements with eleven dogs of the output of epinephrine from the adrenals to determine whether intravenous injection of epinephrine is capable of modifying the rate of secretion. Quantities ranging from ten to 500 times the average amount of epinephrine ordinarily secreted by the adrenals per minute were introduced. The epinephrine concentration in the blood and the rate of secretion were determined by the method of Stewart and Rogoff. In some of the experiments the results were confirmed by the method recently described by Rogoff,[6] in which sensitized eye reactions in cats are employed.

In some of the experiments the epinephrine was administered at a constant rate; in others it was given in a single injection, to simulate the "outburst" from the adrenals that is alleged to occur during emotional excitement. The smallest dose employed, i. e., 0.002 mg. per kilogram of body weight a minute, caused an elevation of blood pressure during the injection in anesthetized dogs; striking reactions in the blood pressure were produced by the larger doses.

For constant injection we employed an apparatus devised by one of us (J. M. R.). The essential construction of the device includes a constant speed motor which drives a nuggled disk by a hard rubber friction drive; the disk operates a pinion and gear reduction to a screw which is kept in constant motion, propelling forward the piston of one, two or three syringes. When syringes with a capacity of 50 cc. are used, adjustment can be made so that any quantity between 0.7 cc. and 7.5 cc. a minute can be delivered at a constant rate of flow against any pressure that might be met in the blood vessel. Further alteration of the range of quantities delivered can be accomplished by employing syringes of different capacity.

The results of our experiments on the rate of liberation of epinephrine from the adrenal glands under the influence of intravenous administration of epinephrine are illustrated in the following condensed protocols:

EXPERIMENT 1.—In a male dog weighing 14.1 Kg. a cava pocket was prepared with the aid of urethane anesthesia. When the first specimen of adrenal blood was obtained, the blood flow was 22 Gm. a minute and the blood pressure 110 mm. of mercury. Constant intravenous injection of 0.028 mg. of epinephrine a minute was performed for three minutes (corresponding to ten times the normal average rate of adrenal secretion); the maximum blood pressure was 118 mm. The second specimen of adrenal blood was obtained immediately after the injection; the blood flow was 13.9 Gm. a minute and the blood pressure from 108 mm. to 94 mm. The third specimen of adrenal blood was obtained during electrical stimulation of the branchial nerve. Quantitative assay was unsatisfactory; differences between an epinephrine concentration of 1: 5,000,000 and one of 1: 10,000,000 were not detectable with the test object. All three specimens were found to have a concentration within this range, indicating qualitatively a normal output and no significant influence exerted by injected epinephrine or by sensory stimulation.

EXPERIMENT 2.—In a dog weighing 10.25 Kg. a cava pocket was prepared with the aid of pentobarbital sodium anesthesia. When the first specimen of adrenal blood was obtained the blood flow was 14.6 Gm. a minute. Constant intravenous injection of 0.04 mg. of epinephrine a minute was performed for one minute (corresponding to twenty times the normal average rate of adrenal secretion). The second specimen of adrenal blood was obtained immediately after the injection; the blood flow was 10.5 Gm. a minute. Twenty-five minutes later, constant injection of 0.04 mg. of epinephrine for one minute was repeated, and immediately thereafter the third specimen of adrenal blood was obtained. The blood flow was 8.25 Gm. a minute. The first specimen was assayed at an epinephrine concentration 1: 6,500,000, corresponding to an output of 0.00224 mg. a minute for the dog, or 0.00022 mg. per kilogram a minute. The second specimen was assayed at a concentration of 1: 5,000,000 and the third at a concentration of 1: 4,000,000, both concentrations corresponding to an output of 0.0021 mg. a minute for the dog, or 0.0002 mg. per kilogram a minute.

EXPERIMENT 3.—In a dog weighing 8.75 Kg. a cava pocket was prepared with the aid of pentobarbital sodium anesthesia. When the first specimen of adrenal blood was obtained, the blood flow was 10.7 Gm. a minute and the blood pressure 132 mm. of mercury. Constant intravenous injection of 0.036 mg. of epinephrine was performed for one minute (corresponding to twenty times the normal average rate of adrenal secretion). The second specimen of adrenal blood was collected during one minute, beginning thirty seconds before the end of the injection; the blood flow was 9.5 Gm. a minute and the maximum blood pressure 156 mm. The first specimen was assayed at an epinephrine concentration of approximately 1: 50,000,000, corresponding to an output of 0.000214 mg. a minute for the dog, or 0.000024 mg. per kilogram a minute. The second specimen was assayed at a concentration of approximately 1: 20,000,000, corresponding to an output of 0.00047 mg. a minute for the dog, or 0.000053 mg. per kilogram a minute.

EXPERIMENT 4.—In a female dog weighing 7 Kg. a cava pocket was prepared with the aid of pentobarbital sodium anesthesia. The blood pressure was 112 mm. of mercury. Constant intravenous injection of 0.07 mg. of epinephrine a minute was performed (corresponding to fifty times the normal average rate of adrenal secretion). The first specimen of adrenal blood was obtained ten minutes after the beginning of the injection; the blood flow was 6.2 Gm. a minute and the maximum blood pressure 182 mm. The second specimen of adrenal blood was obtained twenty minutes after the beginning of the injection; the blood flow was 9.6 Gm. a minute and the blood pressure 142 mm. The first specimen was assayed at an epinephrine concentration of 1: 4,000,000, corresponding to an output of 0.00155 mg. a minute for the dog, or 0.00022 mg. per kilogram a minute. The second of the specimens was assayed at a concentration of 1: 5,000,000, corresponding to an output of 0.00192 mg. a minute for the dog, or 0.00027 mg. per kilogram a minute.

EXPERIMENT 5.—In a female dog weighing 9.35 Kg. a cava pocket was prepared with the aid of urethane anesthesia. The blood pressure was 104 mm. of mercury. A constant intravenous injection of 0.187 mg. of epinephrine a minute was performed (corresponding to 100 times the normal average rate of adrenal secretion). A specimen of adrenal blood was obtained six minutes after the beginning of the injection; the blood flow was 13.98 Gm. a minute and the maximal blood pressure 170 mm. Simultaneously with the collection of the adrenal blood, a specimen of arterial blood was withdrawn from the abdominal aorta. The adrenal blood was assayed at an epinephrine concentration of 1: 1,000,000, corresponding to an output of 0.0139 mg. a minute for the dog, or 0.00148 mg. per kilogram a minute. The epinephrine concentration in the arterial blood was determined to be slightly less than that in the adrenal blood.

EXPERIMENT 6.—In a female dog weighing 9.65 Kg. a cava pocket was prepared with the aid of urethane anesthesia. Constant intravenous injection of 0.386 mg. of epinephrine a minute was performed for two minutes (corresponding to 200 times the normal average rate of adrenal secretion). When a specimen of adrenal blood was obtained just after the injection, the blood flow was 12.3 Gm. a minute and the blood pressure from 210 to 170 mm. of mercury. A specimen of arterial blood was withdrawn from the abdominal aorta thirty seconds after the specimen of adrenal blood was obtained; the blood pressure was 120 mm. The adrenal specimen was assayed at an epinephrine con-

6. Rogoff, J. M.: A Sensitive Method for Quantitative Estimation of Epinephrine in Blood, Proc. Soc. Exper. Biol. & Med. **36**: 441 (May) 1937.

centration of 1:4,000,000, corresponding to an output of 0.003 mg. a minute for the dog, or 0.00031 mg. per kilogram a minute. The epinephrine concentration in the arterial blood was determined to be approximately 1:10,000,000.

EXPERIMENT 7.—In a female dog weighing 8.9 Kg. a cava pocket was prepared with the aid of urethane anesthesia. The blood pressure was 95 mm. of mercury. Constant intravenous injection of 0.54 mg. of epinephrine a minute was performed for two minutes (corresponding to 300 times the normal average rate of adrenal secretion). A specimen of adrenal blood was obtained during the ascent of the blood pressure, which reached a maximum of 205 mm.; the blood flow was 14 Gm. a minute. During the injection and simultaneously with the collection of the adrenal blood, a sample of arterial blood was withdrawn from the abdominal aorta. The blood pressure after the injection fell to 88 mm. The adrenal blood was assayed at an epinephrine concentration of 1:1,500,000, corresponding to an output of 0.00933 mg. a minute for the dog, or 0.00105 mg. per kilogram a minute. The epinephrine concentration in the arterial blood differed but little from that in the adrenal blood.

EXPERIMENT 8.—In a male dog weighing 9.5 Kg. a cava pocket was prepared with the aid of urethane anesthesia. When the first specimen of adrenal blood was obtained, the blood flow was 6.5 Gm. a minute and the blood pressure 68 mm. of mercury. Constant intravenous injection of 1 mg. of epinephrine a minute was performed for two minutes (corresponding to 500 times the normal average rate of adrenal secretion). The second specimen of adrenal blood was obtained within thirty seconds after the injection, while the blood pressure was still at the maxmium height reached, 185 mm.; the blood flow was 15.5 Gm. a minute. The third specimen of adrenal blood was obtained five and one-half minutes after collection of the second; the blood flow was 2.33 Gm. a minute and the blood pressure 40 mm. The first specimen was assayed at an epinephrine concentration of 1:3,000,000, corresponding to an output of 0.0021 mg. a minute for the dog, or 0.00022 mg. per kilogram a minute. The second specimen was assayed at a concentration of 1:500,000, corresponding to an output of 0.031 mg. a minute for the dog, or 0.0032 mg. per kilogram a minute. The third specimen was assayed at a concentration of 1:5,000,000, corresponding to an output of 0.00047 mg. a minute for the dog, or 0.00005 mg. per kilogram a minute.

EXPERIMENT 9.—In a female dog weighing 8.5 Kg. a cava pocket was prepared with the aid of urethane anesthesia. When the first specimen of adrenal blood was obtained, the blood flow was 16.9 Gm. a minute and the blood pressure 80 mm. of mercury. Intravenous injection, a single dose of 0.5 mg. of epinephrine, was performed (corresponding to 300 times the normal average adrenal output a minute). The blood pressure rose to a maximum level of 188 mm. The second specimen of adrenal blood was obtained during the return of the blood pressure; the blood flow was 12.25 Gm. a minute and the blood pressure at the end of the collection 56 mm. The third specimen of adrenal blood was obtained fifteen minutes after the second; the blood flow was 13.2 Gm. a minute and the blood pressure 58 mm. The three specimens showed but little difference in epinephrine concentration; they were assayed at a concentration of 1:4,000,000, corresponding to outputs of 0.004 mg., 0.0031 mg. and 0.0033 mg. a minute for the dog, or 0.00048 mg., 0.00036 mg. and 0.00039 mg. per kilogram a minute for the first, second and third specimens, respectively.

EXPERIMENT 10.—In a male dog weighing 9.5 Kg. a cava pocket was prepared with the aid of urethane anesthesia. When the first specimen of adrenal blood was obtained the blood flow was 11.4 Gm. a minute and the blood pressure 88 mm. of mercury. Intravenous injection, a single dose of 0.8 mg. of epinephrine, was performed (corresponding to 450 times the normal average adrenal output per minute). The blood pressure rose to a maximum of 175 mm. The second specimen of adrenal blood was obtained during the period of elevated blood pressure; the blood flow was 16.6 Gm. a minute. The third specimen of adrenal blood was obtained seven minutes later; the blood flow was 7.1 Gm. a minute and the blood pressure 67 mm. The first specimen was assayed at an epinephrine concentration of 1:5,000,000, corresponding to an output of 0.00228 mg. a minute for the dog, or 0.00024 mg. per kilogram a minute. The second specimen was assayed at a concentration of 1:3,000,000, corresponding to an output of 0.0055 mg. a minute for the dog, or 0.00057 mg. per kilogram a minute. The third specimen was assayed at a concentration of 1:4,000,000, corresponding to an output of 0.00177 mg. a minute for the dog, or 0.000186 mg. per kilogram a minute.

EXPERIMENT 11.—In a male dog weighing 10.25 Kg. a cava pocket was prepared with the aid of pentobarbital sodium anesthesia. When the first specimen of adrenal blood was obtained the blood flow was 9.65 Gm. a minute and the blood pressure 104 mm. of mercury. Intravenous injection, a single dose of 1 mg. of epinephrine, was performed (corresponding to 500 times the normal average adrenal output a minute). The blood pressure rose to a maximum level of 225 mm. The second specimen of adrenal blood was obtained during the ascent of the blood pressure; the blood flow was 10 Gm. a minute. Quantitative assay of the epinephrine concentration in the first specimen was not satisfactory; qualitatively, this specimen was much weaker than the second. The second specimen was assayed at an epinephrine concentration of 1:750,000, corresponding to an output of 0.0133 mg. a minute for the dog, or 0.0013 mg. per kilogram a minute.

The evidence derived from these experiments is against the probability of an autogenous continuance of adrenal secretion produced by circulating epinephrine. Constant intravenous administration of epinephrine, in amounts comparable to the rate of adrenal secretion under powerful stimulation, did not alter the output of epinephrine from the glands, although elevation of blood pressure occurred in every instance; nor was the epinephrine concentration in the blood of the adrenal vein different from that usually found in normal dogs under ordinary experimental conditions.

Increase in the rate of secretion of epinephrine up to twenty or thirty times the normal rate can be produced by electrical excitation of the splanchnic nerves[7] or by the action of certain drugs.[8] In dogs 1, 2, 3 and 4, quantities of epinephrine up to fifty times the normal average amount liberated by the adrenals were administered.

For some unknown reason the initial output of epinephrine in dog 3 was exceedingly low. Nevertheless, although the calculated output during the injection of epinephrine is double the initial output, the latter was not even increased to a level approaching the normal rate of liberation. It has been found that an increase can be accomplished by splanchnic stimulation under similar circumstances.[9] It would seem that a low rate of secretion should be favorable for obtaining an increase, especially when the stimulus presumably would act on the peripheral secretory mechanism.

When the rate of blood flow through the adrenals is not diminished, an increase in the concentration of epinephrine indicates augmentation of the rate of liberation. In these experiments, however, the increased concentration of epinephrine in the blood of the adrenal vein may have been due chiefly, if not entirely, to the injected epinephrine in the circulation. Owing to the relatively high rate of blood flow through the adrenals, the blood of the adrenal vein is largely arterial and, to a certain extent, reflects the epinephrine concentration in the arterial blood; therefore, when large quantities of epinephrine are injected, the increased concentration may lead to an erroneous interpretation of increased

7. Stewart, G. N., and Rogoff, J. M.: Effect of Stimulation of Afferent Nerves upon the Rate of Liberation of Epinephrine from the Adrenals, Am. J. Physiol. **69:** 605 (Aug.) 1924.

8. Stewart, G. N., and Rogoff, J. M.: The Action of Drugs upon the Output of Epinephrine from the Adrenals: Strychnine, J. Pharmacol. & Exper. Therap. **13:** 95 (May) 1919; The Action of Drugs upon the Output of Epinephrine from the Adrenals: Nicotine, ibid. **13:** 361 (July) 1919.

9. Rogoff, J. M., and Nixon, E. Nola: Epinephrine Output from the Adrenals in Experimental Diabetes, Am. J. Physiol. **120:** 440 (Nov.) 1937.

rate of secretion by the adrenals. This possibility is demonstrated by the results obtained in the dogs receiving massive doses of epinephrine.

Thus, in dogs 5 and 7, specimens of blood from the adrenal vein were collected while large amounts of epinephrine were being introduced into the circulation; arterial blood, taken from the aorta, was obtained simultaneously with the collection of adrenal blood. The epinephrine concentration was practically the same in the arterial and in the adrenal blood, and the calculated output from the adrenals appeared higher than normal. In dog 6, however, adrenal blood taken after the injection of a large dose of epinephrine showed but little, if any, increase in output; arterial blood taken shortly thereafter showed an epinephrine concentration too low to modify significantly the calculated output from the adrenals.

Similar results were obtained in the animals (dogs 9, 10 and 11) to which large amounts of epinephrine were administered in single injections, to simulate an outburst from the adrenals. The apparent increase in the output of epinephrine was in every case due to the fact that there was a large amount of circulating epinephrine for a brief period after the injection, for only those specimens of adrenal blood which were collected during the period of pressor activity of the injected epinephrine showed a calculated increase in output from the adrenals.

Of course, although the epinephrine concentration in the arterial blood roughly paralleled that of the adrenal blood, it would be difficult to maintain that a small increase in output is not included in the calculated, apparent increase. However, if such an increase does occur it is brief, for as soon as the pressor effect of the injected epinephrine subsides it is no longer possible to demonstrate an apparent increase in output from the adrenals. Indeed, our experiments indicate the probability that immediately after the hemodynamic effects of the injected epinephrine there is a brief period of diminished output of epinephrine from the adrenals (dogs 8 and 10), the output returning to the original level within fifteen minutes (dog 9).

If epinephrine is capable of exerting an inhibitory action on the adrenal medulla, Elliott's[10] observation that the store of epinephrine in the adrenal is diminished after injections of epinephrine might be explained by a possible inhibitory influence on the rate of production. At any rate, diminished store alone is not adequate evidence of increased liberation of epinephrine from the adrenals; at most it affords information on the balance between production and liberation.

QUANTITATIVE EXPERIMENTS ON THE DURATION OF EFFECTIVE CONCENTRATIONS OF EPINEPHRINE IN THE SYSTEMIC CIRCULATION

The brief hemodynamic effect of a single intravenous injection of epinephrine is well known. In view of the subject under investigation, we performed thirty-two quantitative experiments, on fifteen dogs, to determine whether some of the injected epinephrine might be retained in the blood longer than the period corresponding to its pressor action, especially when relatively large amounts are administered constantly over a long period.

Epinephrine was introduced intravenously in amounts equivalent to the increased quantities secreted from the adrenals under powerful stimulation.[11] From ten to fifty times the average amount normally secreted by the adrenals was administered at a constant rate of injection. Systemic blood was obtained at intervals during and after the injections, which were continued for periods ranging from thirteen to ninety-four minutes, from anesthetized and nonanesthetized animals.

In most of these experiments we used the serum instead of defibrinated blood for determination of the epinephrine concentration. This is advantageous when the concentration is low, since it has been found that all the epinephrine in the blood is in the serum or the plasma.[12] Thus, a concentration too weak for detection in the blood often may be detected quantitatively in the serum, in which the concentration is approximately twice as great. Specimens of blood were obtained (*a*) from the left ventricle or the femoral artery, (*b*) simultaneously from the abdominal aorta and the vena cava, (*c*) simultaneously from the right ventricle and the femoral artery and (*d*) from both ventricles, from one to three minutes apart, the order of collection being reversed in different experiments.

We found that intravenously injected epinephrine disappears from the circulation so rapidly that it is rarely detectable in the blood beyond the period of its pressor action. These results, on dogs, confirm the unpublished results on cats, obtained earlier by Rogoff and Wasserman at Western Reserve University. In both dogs and cats, when single injections of amounts up to about ten or fifteen times the average normal output of the adrenals a minute have been given, epinephrine can no longer be detected in the systemic (arterial) circulation after one complete circuit of the blood. This is true also when such amounts are injected constantly over relatively long periods; as soon as the injection is stopped and the blood pressure returns to the original level, the epinephrine cannot be found in the blood with sensitive test objects. When a quantity equal to from twenty-five to fifty or more times the average normal output of the adrenals a minute is administered in a single injection, approximately one half or one fourth of the epinephrine may be detected in arterial blood obtained within one-half or one minute after the injection.

Rarely was an epinephrine reaction produced by the serum when blood was obtained two or more minutes after a single injection of epinephrine, although sensitive test objects were often available. When large amounts of epinephrine were injected at a constant rate for an hour or longer, a small reaction was occasionally observed for some minutes (in one instance up to twenty minutes) after the end of the injection. However, prolonged administration of such large doses is not well tolerated by the animals.

Our experiments demonstrate that epinephrine disappears rapidly from the systemic blood when it is introduced into the circulation in amounts equivalent to those liberated by the adrenals under strong stimulation. For example, epinephrine was injected intravenously at a constant rate of 0.038 mg. a minute in a dog weighing 12.8 Kg. Arterial blood obtained twenty-two minutes after the beginning of the injection contained an epinephrine concentration of approximately 1 : 200,000,000. A specimen obtained shortly after the end of the injection was assayed at an epinephrine concentration of less than 1 : 800,000,000. In twenty-two minutes 0.836 mg. of epinephrine entered the blood stream; if all of it

10. Elliott, T. R.: The Action of Adrenalin, J. Physiol. **32**: 401, 1905; The Control of the Suprarenal Glands by the Splanchnic Nerves, ibid. **44**: 374, 1912.
11. Stewart and Rogoff, footnotes 7 and 8.
12. Stewart, G. N., and Rogoff, J. M.: The Proportion in Which Adrenalin Distributes Itself Between Corpuscles and Serum in Relation to the Technic of Testing for Epinephrine in Blood, J. Pharmacol. & Exper. Therap. **14**: 79, 1917.

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had been retained in the circulation there should have been an epinephrine concentration of nearly 1:1,000,000 in the arterial blood. Thus more than 99 per cent of the epinephrine disappeared from the blood in the systemic circulation during the injection.

Assay of specimens of blood collected simultaneously from the abdominal aorta and the vena cava during constant intravenous (external jugular vein) injection of epinephrine in amounts equal to from fifteen to thirty times the average normal quantity of adrenal secretion showed a loss of approximately half of the epinephrine from the arterial blood while it was passing to the venous side of the vascular system. A similar loss of epinephrine was observed in the blood coursing through the pulmonary circuit.

Unless it can be proved that there is an impairment in the capacity for removing epinephrine from the circulation in hypertension, it is highly improbable, in the light of these quantitative observations, that hypersecretion of epinephrine by the adrenals and presence of epinephrine in the systemic circulation in concentrations capable of producing a persistent elevation of blood pressure can be a cause of chronic hypertension. Such concentrations, if present, could be detected by our methods.

Reports in the literature alleging that epinephrine was detected in the systemic circulation in cases of various conditions may be said to have been based on improper use of methods or use of improper methods. Incredible concentrations have been reported; in some cases, simple arithmetical calculation would show the improbability, if not impossibility, of the existence of such epinephrine concentrations in the circulating blood. In 1931 Rogoff and Wasserman [13] tested systemic blood from a small group of patients with hypertension (obtained through Dr. R. W. Scott at Cleveland City Hospital) and were unable to detect epinephrine. Stewart [14] had previously reported similar negative results, using the same method.

A number of other investigators, working with satisfactory but less sensitive methods, failed to detect epinephrine in the systemic blood after the pressor effects of large doses had subsided. The mechanism whereby the epinephrine disappears from the blood is unknown; probabilities are oxidation, fixation or utilization by tissues on which it acts, elimination or a combination of these. Excretion by the kidneys has been suggested, but the alleged detection of epinephrine in urine is based on work with unreliable methods. Jackson [15] found that the duration of the pressor effects of epinephrine is not altered by ligation of the renal blood vessels.

We performed experiments in which acute hypertension was produced by renal ischemia following firm application of Goldblatt's clamps and others in which it was produced by ligation of the renal arteries. Some of the dogs acquired acute uremia, especially those in which the renal arteries were ligated. In some but little hypertension developed, while in others there was considerable elevation of blood pressure. In none of the animals was the rate of secretion of epinephrine from the adrenals different from that ordinarily found in normal dogs. Goldblatt [16] was able to produce chronic hypertension by renal ischemia in dogs after excision of one adrenal and denervation of the other with mechanical destruction of its medulla. This type of hypertension, therefore, apparently is independent of the secretion of epinephrine from the adrenals.

13. Rogoff, J. M., and Wasserman, P.: Unpublished data.
14. Stewart, G. N.: The Alleged Existence of Epinephrine in Pathological Sera, J. Exper. Med. **15**: 547, 1912.
15. Jackson, D. E.: The Prolonged Existence of Adrenalin in Blood, Am. J. Physiol. **23**: 226, 1909.
16. Goldblatt, Harry; Lynch, James; Hanzal, R. F., and Summerville, W. W.: The Production of Persistent Elevation of Systolic Blood Pressure by Means of Renal Ischemia, J. Exper. Med. **59**: 347 (March) 1934.

COMMENT

Existing experimental and clinical evidence is inadequate to support the view that epinephrine secretion is an important factor in the etiology and pathology of chronic hypertension. With the possible exception of conditions arising from the presence of certain types of adrenal medullary neoplasms, the concept of hypersecretion of epinephrine as a cause of persistent elevation of the blood pressure is untenable. Our quantitative experiments contradict the suggestion that an "autogenous continuance" of secretion of epinephrine is possible.

The so-called emergency theory of adrenal function has furnished support to advocates of various ideas and practices in clinical medicine for a quarter of a century. The theory is attractive, but it has been contested severely on the ground that it is not based on unequivocal, quantitative, experimental premises. The present investigation adds to the evidence against the principles supported by this theory.

Serious consequences may arise from premature application of unproved theory to clinical practice. There is a growing tendency among clinicians to resort to surgical intervention at the adrenals or their nerves or to subject the adrenal region to roentgen irradiation in the treatment of hypertension. Damage to the adrenal blood vessels may lead to degeneration and atrophy of the indispensable adrenal cortex.[17] It has been shown that adrenal operations for therapeutic purposes may lead to development of fatal Addison's disease.[18]

In some cases, irradiation of the hypophysis as well as of the adrenals is practiced. If it is assumed that an interrelated function between the hypophysis and the adrenal medulla is involved in such treatment, we may point out that hypophysectomy does not alter the rate of secretion of epinephrine from the adrenals.[19] Page and Sweet [20] produced hypertension by renal ischemia in hypophysectomized dogs; when they performed hypophysectomy after producing hypertension the pressure declined. In 1935 one of us (J. M. R.) collaborated in a portion of the preliminary experiments by Dr. Harry Goldblatt on hypophysectomized dogs. It was found that hypophysectomy does not prevent development of hypertension due to renal ischemia. At any rate, we believe that the experimental basis for intervention at the hypophysis in the treatment of hypertension is even less substantial than intervention at the adrenals.

Our experiments lend no support to the possibility of an accumulation of epinephrine in the circulation in amounts capable of causing sustained elevation of blood pressure. The presence of such quantities of epinephrine in the circulation would produce effects, other

17. Rogoff, J. M.: Experimental Production of Chronic and Subacute Adrenal Insufficiency in Dogs and Cats, Proc. Soc. Exper. Biol. & Med. **29**: 1240 (June) 1932.
18. Rogoff, J. M.: Addison's Disease Following Adrenal Denervation in a Case of Diabetes Mellitus, J. A. M. A. **106**: 279 (Jan. 25) 1936. Snell, A. M.; Wilder, R. M., and Cragg, R. W.: Suprarenal Atrophy Following Denervation: Report of a Case with Findings at Necropsy, J. Path. & Bact. **43**: 473 (Nov.) 1936.
19. Rogoff, J. M.; Nixon, E. Nola; Stewart, George N., and Marcus, Emanuel: Epinephrine Secretion in Hypophysectomized Dogs, Proc. Soc. Exper. Biol. & Med. **37**: 715, 1938.
20. Page, I. H., and Sweet, J. E.: Extirpation of Pituitary Gland on Arterial Blood Pressure of Dogs with Experimental Hypertension, Proc. Soc. Exper. Biol. & Med. **34**: 260 (March) 1936.

than hypertension, which could not be tolerated for more than a relatively short period. We have shown that even large amounts of epinephrine introduced into the circulation disappear from the systemic blood very rapidly. Furthermore, we have demonstrated that an increased concentration of epinephrine in the systemic circulation does not produce a detectable increase in epinephrine secretion from the adrenals. Accordingly, the premise on which rests the theory that hypersecretion of epinephrine is a cause of hypertension is not supported by quantitative measurements of the rate of secretion of epinephrine.

The clinical significance of this investigation is obvious. In our opinion, these experiments support the conclusion that intervention at the adrenals as a method for treating hypertension does not have the support of unequivocal experimental studies. The practice is not without considerable risk to the patient; therefore such heroic measures ought to be deprecated. We agree entirely with the final statement made in an editorial published recently in THE JOURNAL [21] that "the therapeutic hazard in a disorder should not exceed the disease hazard."

INCIDENCE AND CAUSES OF CHRONIC DYSPEPSIA AT VARIOUS AGES

AN ANALYSIS OF 4,223 CASES

ANDREW B. RIVERS, M.D.
AND
ANTONIO E. MENDES FERREIRA, M.D.
Fellow in Surgery, the Mayo Foundation
ROCHESTER, MINN.

Turn on the radio, casually glance through advertisements in papers and periodicals or read the signs which are scattered everywhere along the highways, and it soon becomes evident how important symptoms of dyspepsia have become to the laity. All these advertising mediums give instructions on how to return to gastronomic happiness by easy and inexpensive means. In this paper we shall outline some of the more frequent causes of chronic dyspepsia and submit evidence pointing to the danger, particularly at certain ages, of the layman's attempting to cure himself by taking advertised therapeutic nostrums.

Physicians are in part responsible for this lamentable situation, because a diagnosis of "dyspepsia" is frequently made although, as is well known, this condition is not a disease but only a symptom. In the hope that certain symptoms are transitory and inconsequential, the physician sometimes advises easily available medications which have previously been found to be effective, and sometimes it turns out that serious disease has, because of the dilatory methods of diagnosis, been overlooked. Unfortunately, the severity of digestive disturbances is not necessarily an indication of the extent or gravity of the underlying cause, nor are pathologic processes giving rise to such symptoms limited to diseases of the stomach or duodenum or even to organs directly utilized and concerned in the process of digestion. A great variety of diseases may herald their approach or indicate their presence by causing disturbances in the smooth, rhythmic behavior of the processes of digestion.

21. In Defense of the Adrenals, editorial, J. A. M. A. **106**: 294 (Jan. 25) 1936.

From the Division of Medicine, the Mayo Clinic.

MATERIAL FOR STUDY

To obtain the material for this study, 10,000 consecutive histories of patients aged 15 or older were scrutinized. In the first place we were interested in knowing how many of these patients complained of indigestion. If the complaints included symptoms of dyspepsia, the history was carefully analyzed in order to ascertain the causes of the complaint. A division of histories according to sex was then made and the causes of dyspepsia determined for each sex. We next proceeded to study the causes of dyspepsia in patients who presented themselves primarily because of this condition. Finally, because it is obvious that there must be some variation in the causes and the gravity of diseases responsible for dyspepsia at different ages, the histories were divided into three groups: the first for patients from 15 to 24 years of age, the second for patients from 25 to 39 and the third for patients of 40 and older.

INCIDENCE

A review of the histories in this series attests the fact that one of man's most frequent problems is related to his digestive unhappiness. More than 42 per cent of the patients included complained of dyspepsia, and about half of these presented themselves primarily because of dyspepsia. We were rather surprised to find that dyspepsia was slightly more common among men than among women. Of the 4,223 patients who volunteered the complaint of dyspepsia, 2,147 were males and 2,076 females. Of the male patients who included digestive disturbances among their complaints, 54 per cent came to the clinic primarily to seek aid for this complaint; only 41 per cent of the female patients with indigestion considered this their major ailment.

In chart 1 we have shown the incidence of dyspepsia at various ages for the 10,000 consecutive registrations included in this study. In clinic registrations we found proportionately less dyspepsia among persons less than 30 years of age. Between this age and 60 almost half of the total number of patients had some complaint of

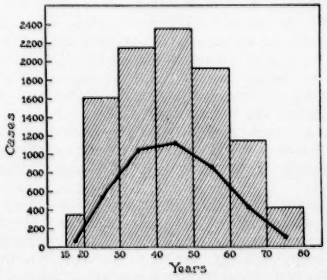

Chart 1.—Incidence of dyspepsia in 10,000 consecutive cases. The black line represents the number of patients with a complaint of dyspepsia and the shaded blocks the total registrations for each age group for the same period.

digestive difficulties. After 60 the relative proportion of patients who complained of indigestion to total registrations for similar ages diminished somewhat. This does not mean, however, that the gravity of the complaint was proportionately less for older persons. In fact, as might be expected, the causes for the dyspepsia were of relatively graver significance for patients beyond the age of 40 than for younger patients.

CLASSIFICATION

It would be confusing to enumerate separately all the heterogeneous maladies responsible for the dyspepsia in this series of 4,223 cases. We therefore intend to indicate the most common causes for the complaint in the various age groups and to list these and the less frequent causes according to the etiologic classification of dyspepsia suggested by Eusterman and Balfour.[1] They divided the causes of dyspepsia into four types: organic, reflex, systemic and functional. Under organic causes of dyspepsia we include diseases or anatomic anomalies involving the tissues of the stomach or duodenum. Among the reflex causes of dyspepsia we include diseases of the appendix, gallbladder, biliary ducts, pancreas or intestine and renal stone or other conditions which reflexly disturb the chemistry or mechanics of the stomach and duodenum. Among the dyspepsias of systemic origin we include those due to

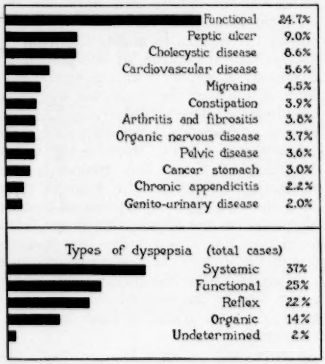

Chart 2.—The twelve most common causes of dyspepsia in order of frequency.

disturbances of metabolism, toxemia, deficiency diseases or dysfunction of the organs of internal secretion. Functional dyspepsias will be assumed to include the disturbances in normal gastroduodenal activity not resulting from demonstrable disease elsewhere in the body. Of this type are the various gastric neuroses, constitutional inadequacies and habit dyspepsias and the various dyspeptic manifestations of chronic nervous exhaustion.

CAUSES OF DYSPEPSIA IN THE SERIES OF 4,223 CONSECUTIVE CASES

A classification of the twelve most common causes of indigestion in order of frequency will be found in chart 2. These twelve causes account for 74.6 per cent of the total number of cases. The remaining causes, a long heterogeneous list, when added to these twelve result in a total incidence as follows: systemic dyspepsia 37 per cent, functional dyspepsia 25 per cent, reflex dyspepsia 22 per cent and organic dyspepsia 14 per cent. In 2 per cent of the cases no diagnosis could be made. Included are all instances of dyspepsia, regardless of whether the condition was the primary or an associated complaint. In a general way the causes of the dyspepsia as indicated in chart 2 are not greatly at variance with those reported by Dwyer and Blackford [2] and by Davis and Vanderhoof.[3]

In chart 3 we have shown the ten most frequent causes of dyspepsia for both males and females. For each sex functional causes remain the most frequent, peptic ulcer being next in importance for the males and cholecystic diseases assuming the same position for the females. Cancer of the stomach was relatively

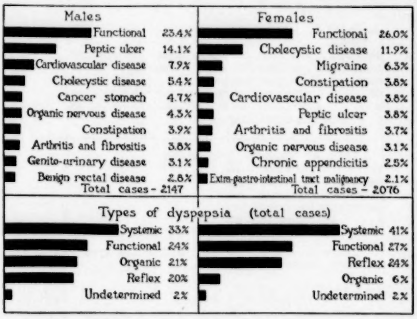

Chart 3.—The ten most frequent causes of dyspepsia according to sex.

important among the males. It is interesting to note that dyspepsia of organic origin was more than three times as frequent in the males as in the females.

Dyspepsia as a Primary Complaint.—The cases thus far considered have included all those of dyspepsia regardless of whether this complaint was considered as of primary or as of secondary importance. Many of the patients came to the clinic for other reasons and during the course of examination mentioned the fact that they also suffered from digestive disturbances. We thought that more accurate information regarding the important causes of dyspepsia could be obtained if we considered separately a group of patients who came to the clinic primarily because of dyspepsia. In chart

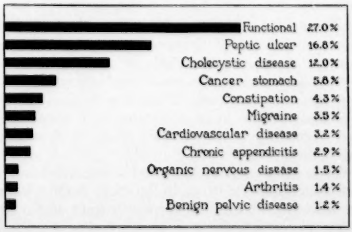

Chart 4.—Causes of dyspepsia in 2,045 cases in which the primary complaint was dyspepsia.

4 are outlined in order of frequency the causes of indigestion in this group, which included 2,045 patients.

The incidence of functional causes in this group was relatively high. Next in importance was peptic ulcer, which accounted for the dyspepsia of about one in six

1. Eusterman, G. B., and Balfour, D. C.: The Stomach and Duodenum, Philadelphia, W. B. Saunders Company, 1935, p. 111.

2. Dwyer, M. F., and Blackford, J. M.: Interpretation of Gastric Symptoms: A Clinical and Roentgenological Study of Three Thousand Cases, Radiology **14**: 38-44 (Jan.) 1930.

3. Davis, T. D., and Vanderhoof, Douglas: A Study of the Causes of Indigestion Based on an Analysis of 4,000 Consecutive Cases, Virginia M. Monthly **53**: 446-448 (Oct.) 1926.

of the total number of patients. About one in eight of the patients was found to harbor cholecystic disease. Of greater importance is the fact that carcinoma of the stomach was the fourth most frequent cause, and it will be remembered that the group includes patients of all ages. It is interesting to note that chronic appendicitis was considered to be the cause of the dyspepsia in only 2.9 per cent of the cases, or only half as frequently as cancer of the stomach.

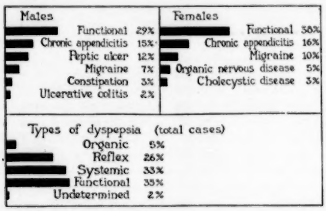

Chart 5.—Causes of dyspepsia in males and females aged from 15 to 24 with a primary complaint of dyspepsia.

Causes of Dyspepsia at Various Ages.—Although in a review comprising all ages it is of academic interest to know what the most common causes of indigestion are, it soon becomes apparent that there must be wide variation in the relative importance of the various causative diseases at different ages. Consider, for example, the incidence of cancer of the stomach. Only 3 per cent of the total of 4,223 dyspeptic patients were found to be suffering from this disease. Obviously the chance of finding cancer as the explanation for chronic dyspepsia in a man over 50 would be far in excess of this figure; actually it would be at least six times greater.

Similarly, functional disturbances which might account for the dyspepsia in a greater number of young patients could hardly be assumed to be of equal etiologic importance in patients beyond the age of 50. Some interesting and important data soon become evident when we review the various causes of dyspepsia at different ages.

Ages from 15 to 24.—In chart 5 are indicated the most frequent causes of dyspepsia in patients in this age group who came to the clinic primarily because of dyspepsia. The sexes are considered separately. A complete analysis was made of all the diseases responsible for indigestion in this group, and these were arranged according to the classification of dyspepsias outlined earlier.

We were rather interested to find the relative importance of functional types of indigestion among young patients whose symptoms of dyspepsia were sufficiently distressing to prompt them to seek relief at the clinic. Chronic appendicitis, although usually considered a disease frequently productive of chronic dyspepsia, was responsible for indigestion about half as frequently as were the functional types of dyspepsia. Peptic ulcer was found to be an important cause of dyspepsia among the males; it was unimportant among the females. Migraine was not an uncommon diagnosis for each sex. Cholecystic disease was of some importance in the causation of dyspepsia, especially among the young female patients.

In addition to the diseases indicated in chart 5 as being the most frequent causes of dyspepsia in this group were many others, such as cardiospasm, nephritis, intestinal infestation with parasites, food allergy, terminal ileitis and, though rare, malignant process of the gastrointestinal tract. It is interesting to note that although these young patients came for examination primarily because of dyspepsia, in only one of twenty instances was the dyspepsia found to be caused by an organic disease of the stomach or duodenum. This is at great variance with the findings for patients of more mature age.

Ages from 25 to 39.—In chart 6 are listed the most frequent causes of dyspepsia in men and women between the ages of 25 and 39 whose primary complaint was indigestion. In this group functional disturbances were still of primary importance. There was only a slight predominance in regard to women. Next in importance for the men was peptic ulcer, which accounted for better than one in four of the cases in this group. The location of the ulcers is of some interest: Ninety-eight were in the duodenum and only one in the stomach. Peptic ulcer was only about a fourth as common among the women as among the men. Cholecystic disease was the cause of indigestion about twice as frequently as peptic ulcer among the women. In 5 per cent of the men the dyspepsia was assumed to be due to disease of the gallbladder.

Migraine and constipation were relatively common causes of dyspepsia. Chronic appendicitis was considered the etiologic factor less frequently among patients in this age group than in younger persons. Cancer of the stomach begins to appear as a causative factor for dyspepsia among the men of this age. Among the 750 women in this group there was no instance of carcinoma of the stomach and only one of cancer of the colon. This is rather significant when one considers the fact that of the men of this age who had indigestion sixteen were found to have cancer of the gastrointestinal tract.

Relatively important, though less common, among the causes of indigestion in the men were gastritis, diseases of the urinary system (especially disease of the kidney and ureteral stone) epilepsy, endocarditis

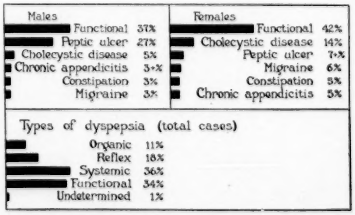

Chart 6.—Causes of dyspepsia in men and women aged from 25 to 39 with a primary complaint of dyspepsia.

and rectal fissure or fistula. Among women the more frequent causes other than those listed were endocarditis, allergy, disease of bone, organic nervous disease (brain tumor and epilepsy), genitourinary disease and hyperthyroidism. General classification of the diseases responsible for the symptoms of dyspepsia in this group reveals the fact that organic disease of the stomach and duodenum was a cause of symptoms more than twice as frequently as in younger patients. Reflex disturbances were less frequent causes than in the

younger group; systemic diseases and functional disturbances accounted for the complaints in 36 and 34 per cent, respectively.

Patients of 40 and Older.—In chart 7 are listed the most frequent causes of dyspepsia in men and women of 40 and older who presented themselves for examination primarily because of dyspepsia. It soon becomes apparent when one considers the cause of dyspepsia in these patients that the condition must be considered as of grave importance. Whereas in the younger age groups functional disturbances were one of the principal causes of dyspepsia, they now begin to assume a role of decidedly less importance.

Approximately one in four of the women in this group was found to have cholecystic disease; peptic ulcer remained a disease of importance, and cancer of the gastrointestinal or the accessory gastrointestinal tract was found to account for the dyspepsia of 5.8 per cent of the women. Cardiovascular disease was a relatively frequent cause. Cancer of the stomach, although less frequently the cause of indigestion in the women than in the men of this age group, nevertheless

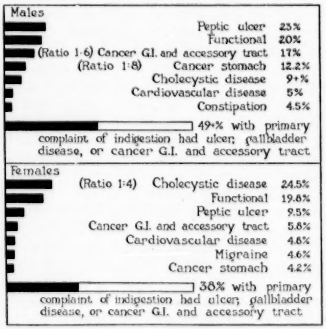
Males
Peptic ulcer 25%
Functional 20%
(Ratio 1·6) Cancer GI. and accessory tract 17%
(Ratio 1·8) Cancer stomach 12.2%
Cholecystic disease 9+%
Cardiovascular disease 5%
Constipation 4.5%
49+% with primary complaint of indigestion had ulcer, gallbladder disease, or cancer G.I. and accessory tract
Females
(Ratio 1·4) Cholecystic disease 24.5%
Functional 19.6%
Peptic ulcer 9.5%
Cancer G.I. and accessory tract 5.8%
Cardiovascular disease 4.6%
Migraine 4.6%
Cancer stomach 4.2%
38% with primary complaint of indigestion had ulcer, gallbladder disease, or cancer G.I. and accessory tract

Chart 7.—Causes of dyspepsia in men and women of 40 or older who had a primary complaint of dyspepsia.

was a formidable etiologic factor. Another disease frequently responsible among the women was migraine. Appendicitis was considered responsible in only 2 per cent of the women. Hyperthyroidism, diaphragmatic hernia and pelvic diseases were other causes. Of the women in this group, therefore, 38 per cent had indigestion which was caused by diseases of the gallbladder, by peptic ulcer or by cancer of the gastrointestinal or the accessory gastrointestinal tract.

The most frequent cause of dyspepsia in the men of this group was peptic ulcer; functional indigestion was next. What seems to us to be of significance is the fact that one in six of all the men of 40 years or more who came to the clinic with the primary complaint of indigestion were found to have cancer of the gastrointestinal or the accessory gastrointestinal tract. One in eight of the men in this group was found to have cancer of the stomach. Cholecystic disease accounted for more than 9 per cent of indigestion in this group and cardiovascular disease for 5 per cent. Other frequent causes of dyspepsia were constipation, migraine, arthritis, syphilis, disease of the rectum, chronic alcoholism, cardiospasm and organic nervous disease. About half of the men of this group were found to have peptic ulcer, cholecystitis or cancer of the gastrointestinal or the accessory gastrointestinal tract.

Classifying the causes of dyspepsia in patients of 40 or older who sought medical aid primarily because of indigestion, we find that in 32 per cent the dyspepsia was due to organic disease of the stomach or duodenum, in 28 per cent was a reflex type of indigestion, in 20 per cent was a functional type and in 18 per cent was due to systemic causes. In 2 per cent of the cases no diagnosis was possible. It is rather a significant fact that more than six times as many patients in this age group as in the group aged from 15 to 24 had organic disease of the stomach or duodenum as the cause of their dyspepsia.

SUMMARY

Dyspepsia is one of the most common of the unpleasant experiences to which man is heir. About half of 10,000 patients between the ages of 30 and 60 complained of varying degrees of digestive difficulties.

Chronic Appendicitis.—The causal relationship of the chronically inflamed appendix to recurring dyspepsia has been the subject of much controversy. As a cause of dyspepsia it was considered of importance in only 2.2 per cent of the 4,223 cases included in this series. Most of the patients were young; appendicitis was assumed to be the cause of the indigestion in 15 per cent of the young males between 15 and 24 and in 16 per cent of the females of the same age. In many the condition should probably more accurately have been classified as subacute appendicitis. There was a sharp drop in the incidence of this disease among patients between the ages of 25 and 39, the incidence for this group being 3 plus per cent for men and 4 plus per cent for women. In only 2 per cent of the women older than 39 who came to the clinic primarily because of indigestion was chronic appendicitis considered the cause of the complaint. In only seven of the 1,377 men of this age group did chronic dyspepsia seem explainable on the basis of chronic appendicitis. Though appendicitis may occasionally produce a periodically reappearing indigestion, it would seem to us that appendectomy for this cause after the age of 25 usually produces a therapeutic result disappointing equally to the patient and to the surgeon.

Functional Dyspepsia.—The stresses of life in this day and age exact quite a toll among those who choose to participate vigorously in its race. The resulting nervous and physical exhaustion, worry, depression and various psychic insults not infrequently produce changes in the normally smooth, rhythmic behavior of the chemical and motor mechanics of digestion, and the incident disturbances of function cause dyspepsia. It is not surprising that the highest incidence of functional disturbance in indigestion should occur between the ages of 25 and 39. Almost half of the women of this age who presented themselves primarily because of dyspepsia had dyspepsia of the functional type. The incidence of functional dyspepsia among the men of this age was also high, 37 per cent. Functional types of indigestion were also common among patients between the ages of 15 and 24; 29 per cent of the men and 38 per cent of the women were considered to have a functional type of indigestion. After the age of 40 the relative importance of functional dyspepsia became less, mainly because by this time more significant diseases had developed.

Peptic Ulcer.—This was second in frequency as a cause of dyspepsia among the 4,223 patients. Among men older than 39 who came for examination because

of indigestion it was the most frequent cause of dyspepsia. According to sex, peptic ulcer was four times as common among men as among women. The ulcers were predominantly duodenal. Gastric ulcer predominated among young males and among women beyond the age of 40; duodenal ulcer predominated in men between the ages of 25 and 40. Recurrent dyspepsia should always bring up for differential consideration the possibility of peptic ulcer.

Cholecystic Disease.—Disease of the gallbladder was one of the most common causes of dyspepsia. Among women it was surpassed in frequency only by functional disturbances. Among women past 39 it was the most common cause. There was less than half as much cholecystic disease among men as among women. Even among men, however, it was a frequent cause of indigestion, being fourth in order of frequency among the total number of patients comprising the series. One in eight of all women between the ages of 25 and 39 who presented themselves because of indigestion was found to have disease of the gallbladder. It was found to be the cause of indigestion in women older than 39 in about every fourth case. Although much less common among the causes of dyspepsia in young men and women, it was found to account for indigestion in 1.4 per cent of the males and in 3 per cent of the females.

Cancer.—Although not the most common among the causes of indigestion, cancer is certainly the most important. Failure to recognize cholecystic disease or peptic ulcer is a lamentable mistake; failure to recognize cancer is a fatal error. The incidence of cancer of the stomach in the 4,223 cases was 3 per cent. If we scrutinize these cases more carefully and consider the incidence of cancer of the stomach among patients whose salient complaint was dyspepsia, we find that the probability of the presence of this disease has almost doubled. If we then separate these cases further and consider the importance of cancer as a cause of indigestion among men of 40 or older who considered dyspepsia their major difficulty, we discover the startling fact that one in six had cancer of the gastrointestinal or the accessory gastrointestinal tract. One in eight actually had cancer of the stomach. Even men of this age who came for other causes but who also had some minor difficulties affecting their digestive tract were found to have cancer of the gastrointestinal or the accessory gastrointestinal tract in 4.8 per cent of cases. Cancer as a cause of the indigestion was relatively less common among the women. In the 4,223 cases there was no instance of gastric cancer among women less than 40 years of age. Above that age cancer of the stomach was found in 4.5 per cent of the women who came to the clinic because of dyspepsia, about a third as frequently as among the men.

CONCLUSIONS

Symptoms of chronic dyspepsia must always be evaluated carefully. All available methods of diagnosis should be utilized to obtain exact knowledge regarding its underlying cause. This is particularly important if the patient has reached the age of 40 years, when dyspepsia must be considered of grave significance until it is proved otherwise. Physicians seem to be especially dilatory and procrastinating regarding their own personal dyspeptic experiences, assuming some sort of professional immunity to gastrointestinal disease which may be very grave. This accounts for the fact that cancer of the stomach is detected no earlier among them than among their patients.

It would seem to us that the layman must be educated to realize the risk he takes when, with advancing age, he seeks relief for an ailing stomach by taking the advice of some radio announcer, drug clerk or other vendor of therapeutic nostrums.

THE CUTANEOUS HISTAMINE REACTION AS A TEST OF PERIPHERAL NERVE FUNCTION

LEWIS H. LOESER, M.D.
NEWARK, N. J.

Histamine has come into use as a test for circulatory function in the extremities and as a drug of more general usage. Since the work of Sollmann and Pilcher,[1] Eppinger [2] and Hess [3] and under the influence of the experimental work of Lewis,[4] the drug has taken its place in several fields of medical practice. Its use as a test of circulatory function and as a stimulant of gastric secretion is too well known to need description.

The cutaneous reaction to histamine is a triple response consisting of (1) a purple spot at the site of the puncture; this is usually obscured quickly by (2) the formation of a wheal, (3) the later appearance of an extended area of arterial dilatation—the flare. The ultimate picture closely resembles a mosquito bite—a wheal surrounded by a flare of redness averaging from one-half to 2 inches (1.3 to 5 cm.) in diameter. It is in the flare that my interest centers.

Until 1927, when Sir Thomas Lewis [4] published his monograph, a clear understanding of the physiology of the cutaneous histamine reaction was lacking. Much speculation and theory existed. Bruce [5] in 1910 had observed that when the cutaneous nerve was degenerated no flare reaction was found. He postulated the presence of an "axon reflex" by which a stimulus would travel up one branch of a sensory nerve and down another branch to adjacent parts of the skin without utilizing a nerve cell in the entire reflex. His observations on the reactions of the conjunctiva to mustard oil apparently confirmed this view.

Müller [6] in 1913 observed that the flare was absent in a number of injuries to the spinal cord, at a point corresponding to the site of the injury. He came to the conclusion that the flare was dependent on a spinal reflex arc, mediated through the pathway of the spinal cord as well as through the peripheral nerves. His views influenced others, notably Ebbecke [7] and Krogh,[8] who came to the same conclusion after similar experiences. These workers, including Müller, failed to take into account the probable injury to the nerve roots and ganglions in destructive lesions of the spine.

Lewis and his co-workers, dissatisfied with the current speculation on this subject, proceeded to investigate the phenomena. As a result of their work, certain facts were made clear:

1. The wheal develops as a local reaction to the irritant drug and is independent of the nerve supply.

1. Sollmann, Torald, and Pilcher, J. D.: Endermic Reactions, J. Pharmacol. & Exper. Therap. **9**: 309 (March) 1917.
2. Eppinger, Hans: Ueber eine eigentumliche Hautreaktion, hervorgeufen durch Ergamin, Wien. med. Wchnschr. **63**: 1413, 1913.
3. Hess, R. W.: Die Regulierung des Blutkreislaufes, Leipzig, Georg Thieme, 1930.
4. Lewis, Thomas: The Blood Vessels of the Human Skin and Their Responses, London, Shaw & Sons, 1927.
5. Bruce, A.: Archiv. f. exper. Pathol. u. Pharmakol. **63**: 424, 1910.
6. Müller, L. R.: Deutsche Ztschr. f. Nervenh. **47-48**: 413, 1913.
7. Ebbecke, U.: Die lokale Gefassreaktion der Haut und der inneren Organe, Arch. f. d. ges. Physiol. **169**: 1, 1917.
8. Krogh, August: The Anatomy and Physiology of Capillaries, Yale University Press, New Haven, Conn., 1922.

2. The flare is a local phenomenon which is not immediately abolished by regional anesthesia or by section of the peripheral nerve. It is of neural origin and depends on a purely local nervous reflex. The reflex is, however, dependent on the integrity of the peripheral sensory nerve. After section of the nerve, from six to eight days being allowed for degeneration to set in, the flare is no longer obtained. Section of the nerve at any point from the spinal ganglion to the skin will abolish the flare after sufficient time has elapsed to allow the nerve to degenerate.

These facts have not been utilized in actual practice. Neurologists in particular should have noted these experiments and adapted them to their needs. Here is a simple test, easy to interpret, requiring no laboratory equipment. While the interpretation is restricted to the integrity of the peripheral sensory nerves, by implication and deduction a wide field of usefulness is uncovered. Other than the cranial nerves, the peripheral nerves in the body are mixed nerves, carrying both motor and sensory fibers, so that the integrity of the nerve as a whole can be tested by determining the status of the sensory fibers.

TECHNIC OF TESTING

I have used histamine hydrochloride in 1:1,000 solution. The solution is kept in rubber stoppered vials and apparently does not deteriorate at room temperature over a period of months. Two methods of injection are used. In one I employ a tuberculin syringe and fine hypodermic needle. With this an amount as small as 0.01 cc. is sufficient when injected intradermally. The other method utilizes a spring punch device originally devised for obtaining a drop of blood for blood counts. The blade has been ground down so that only a fine puncture is made into the skin. The initial drop of blood is wiped away and a drop of histamine solution is deposited by contact over the puncture. This can be wiped away after contact of a few minutes.

The injections are made from 1 to 3 inches (2.5 to 7.5 cm.) apart across the area to be tested. By careful choice of sites a definite area can be outlined. In some cases only a single injection is necessary to confirm the clinical observations. In testing for segmental levels a single row of injections, about 1 inch apart, will suffice.

The test should be done quickly so that too much time does not elapse between the first and the last injection. One can then compare the various responses.

The reactions, for clinical purposes, are graded from 0 to 4 plus, according to the amount and intensity of the flare. A wheal with no flare is graded as zero (0). A wheal surrounded by an intense flare about the size of a half dollar (30 mm.) is graded 4 plus. Responses differ in certain parts of the body. Familiarity with the test increases the accuracy of the interpretations.

Variations in reaction are seen. Irregular or patchy flares are frequently seen in partly degenerated or in regenerated nerves after injury. The wheal should form within twenty seconds to one minute. The flare, which is the important factor in the test, appears later, reaches its height in from three to five minutes and begins to fade after from seven to ten minutes. Variations from the normal include delay or decrease in extent or time of reaction. This may be caused by: (*a*) partial degeneration of the peripheral nerve, (*b*) interference with the vascular supply of the area tested and (*c*) errors in technic of injection.

Tests should not be performed on those parts of the skin in which circulation is deficient. This applies not only to extremities with diseased blood vessels but also to the selection of sites at which the skin is normally under pressure, such as in the neighborhood of joints or over the malleoli.

During the past three years I have found the histamine test useful in a wide variety of cases. In many instances the test merely confirms conclusions made obvious by clinical observation. Occasionally it acts as a visible means of demonstrating conclusions to others who might otherwise remain unconvinced. In a few cases this test has been of extreme diagnostic importance.

The histamine test for peripheral nerve function has been found to be of value along the following lines:

1. To determine the presence of degeneration and later regeneration in peripheral nerves following injury. Traumatic lesions to nerves, sufficient in extent to interrupt the integrity of the peripheral nerve, will abolish the flare reaction after from six to eight days has elapsed. In my experience, the absence of flare frequently precedes the electrical reaction of degeneration by several days. Conversely, the flare begins to return in the area supplied by the regenerating nerve considerably earlier than the electrical reactions begin to change. In this way this technic is useful in determining the extent and duration of peripheral nerve injury.

2. To differentiate hysterical from organic anesthesia. Certain cases of hysterical anesthesia closely simulate organic anesthesia, and even the expert occasionally finds the problem perplexing. Not all physicians are skilled in this field, and the problem for the unskilled is not at all simple. The histamine reaction in which from six to eight days is allowed to elapse for degeneration is an effective test in this group of cases; particularly in medicolegal work, in which, following repeated examinations, anesthesias are frequently seen closely simulating the organic.

The test is also of value in those cases in which an actual organic anesthesia is present with a superimposed hysteria. In these cases, the sensory tests, being dependent on the cooperation of the patient, are frequently unreliable. The histamine test provides an accurate method of delimiting the true extent of anesthesia and is obviously independent of the patient's subjective response.

3. To differentiate the sensory anesthesias of malingering from the organic. The problem here is quite similar to that in hysteria. The neurologist of today is not infrequently asked to examine litigants who have been carefully coached and advised as to their symptoms. Complaints of anesthesia are not uncommon following injuries to the trunk and extremities. The histamine test demonstrates in a convincing manner the absence or presence of true dermal anesthesia.

4. As an additional aid in the localization of lesions of the spinal cord. In expanding lesions and in some compressing lesions of the spinal cord there is occasionally interference with the function of the ganglion of the posterior root. If two or more ganglions are involved, a segmental area of the skin at the upper level of the lesion will give a negative response to histamine. This has been demonstrated in one case presenting a tumor of the spinal cord and in several cases presenting fractured vertebras with compression of the cord. Müller [6] used the histamine test for this purpose as far back as 1913.

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5. In the differentiation of nerve root from spinal cord involvement. This differentiation is particularly valuable in lesions of the lower part of the spine where it is necessary to distinguish between lesions of the cauda equina and lesions of the lower part of the spinal cord. The histamine test is negative (no flare) in the anesthetic area when the lesion involves the nerve roots but is normal if the anesthesia is the result of injury to the spinal cord.

6. To demonstrate to skeptical observers, laymen and the like, the presence or absence of anesthesia of peripheral nerve origin. When normal control areas are used the demonstration is very convincing, particularly in cases in which a negative reaction on one side can be compared with a positive reaction on the opposite side.

As a result of experience with the histamine reaction as a test of nerve function, I feel that the test is of more than passing value. I present nothing new in thus urging its use, for other observers have utilized the reaction in this manner in previous years. Their conclusions and reports have for the most part been found only in technical publications and have not been put to clinical use. A valuable addition to the armamentarium of the physician has thus been neglected. It is a reliable and simple procedure to test the function of peripheral nerves and, as such, should be more widely utilized.

31 Lincoln Park.

RECURRENT DIARRHEA DUE TO DYSENTERY ORGANISMS

SIDNEY A. PORTIS, M.D.
Consulting Physician, Cook County Hospital
CHICAGO

The frequency of persistent diarrhea, with or without a known history of a previous acute intestinal infection, stimulated me to investigate the etiologic factors associated with this symptom. With apparently negative results from examination of the stool, a fairly large percentage of patients yielded positive agglutinations in the blood serum for one or more of the organisms of the dysentery group in relatively high titers. Agglutinins have long been known to have an immunologic reaction in the patient's serum against the dysentery bacillus.

Davison [1] in 1920 studied a series of 134 cases of bacillary dysentery in children. He used the agglutination test in addition to bacteriologic methods for diagnosis and considered an agglutination of 1 : 50 or above an indication of previous or present dysentery infection. In infants he considered 1 : 20 as suggestive. He found that the maximum titer occurred from the seventeenth to the twenty-first day after the onset of the disease, and the agglutinins continued to be present for from four to six months. Three patients with diarrhea were negative culturally but gave positive agglutinations.

In the same year M'Leod and Ritchie [2] reported on the serum reaction in bacillary dysentery. Eighty-three per cent of their patients from whose stools B. dysenteriae had been isolated gave positive results serologically; 100 normal persons gave negative results, and of 194 patients with diarrhea who gave negative results bacteriologically, 12.8 per cent showed positive agglutinations.

A study of bacillary dysentery in asylum patients was reported by Dawson and Moodie [3] in the following year. Because agglutinations were present only after the fourth week of the disease, they considered the agglutination test of little diagnostic value in acute cases.

A few months later Gardner [4] disproved the work of Dawson and Moodie. He stressed the importance of using standardized suspensions and of finding the normal limits of the antigen by testing it with a group of suspensions from normal persons or against a previously tested suspension.

In 1922 Patterson and Williams [5] reported some observations on dysentery bacilli of the Sonne type and concluded that the agglutination test was extremely valuable in the diagnosis of chronic bacillary dysentery. They considered a titer of 1 : 80 or above as indicative of an etiologic connection.

Widowitz [6] in 1923, after working on the agglutinations of dysentery bacilli in children, came to the conclusion that the formation of agglutinins is a definite indication of present or previous infection and that so-called normal agglutinins are remnants of real agglutinins.

Agglutination tests with Flexner dysentery bacilli were run on 161 blood specimens from tuberculosis suspects and on thirteen from normal persons. The results were reported by Hull and Henkes [7] in 1923. The specimen from only one of the normal persons was faintly positive. They concluded that persons in the incipient stage of tuberculosis showed positive agglutination with the Flexner bacillus while those in the advanced stage did not react.

The Aberdeen epidemic of milk-borne bacillary dysentery was studied by Kinloch [8] in 1923. By means of the agglutination test he was able to detect a carrier who had played an important role in the spread of the disease.

In 1923 Gardner,[9] after working on the agglutination standard in bacillary dysentery, stated that one or more repetitions of the test at intervals of from three to four days was the best way to establish the presence of an infection.

Major Ash [10] in 1923, in discussing the diagnosis of bacillary dysentery, stated that serologic studies should be done but are not very dependable.

In the next year Guimarães [11] worked on the serodiagnosis of bacillary dysentery and got very favorable

Acknowledgment is made to Eli Lilly & Co. for their assistance and material in this research.
From the Cook County Hospital and the Department of Medicine of Rush Medical College of the University of Chicago.

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results. He found it especially valuable in ruling out colitis and typhoid.

In 1924 Petrie [12] reported on the diagnosis of dysenteric infections in patients in mental hospitals. Although he believed that the agglutination test was inconsistent, he found it helpful in diagnosing chronic cases and in detecting carriers and thought it should be a routine procedure in such institutions.

Widowitz [13] in 1924 reported some additional work on dysentery agglutination in children and found that the blood of even very young infants produces specific agglutinins. He stated that a positive reaction definitely proves a present or past infection.

In 1925 Hilliard [14] reported a careful study of dysentery on patients in mental hospitals. He found that typhoid vaccine increased the agglutinating titer against the Flexner bacillus for about one month. He found the agglutination reaction well defined by the end of two months and persistent thereafter.

Fyre [15] in 1927 investigated an epidemic of Sonne dysentery. He used the agglutination test in addition to cultural methods for diagnosis. He found no significant titer until after the first week.

In 1928 Menton,[16] after examining forty-seven specimens of blood, concluded that a negative agglutination reaction does not exclude bacillary dysentery and that isolation of the organism is essential in diagnosis.

The following year he reported a study of agglutinins to B. dysenteriae in apparently healthy persons.[17] He made 524 tests, and thirty-three persons gave positive reactions. These thirty-three persons all came from crowded sections, and six of them gave histories of previous diarrhea.

Smith and Fraser [18] in 1930 reported the results of agglutination reaction in relation to Sonne dysentery. They studied forty-eight patients with Sonne dysentery and 138 controls and found the test valuable in diagnosis. The percentage of positive reactions was highest after the fifteenth day of the disease.

In the same year de Lavergne, Melnotte and Debenedetti,[19] after a careful study, concluded that the agglutination test was valuable even after many months and that the agglutination titer was always much lower in the control group.

Mackie [20] in 1932 reported that the agglutination test was sometimes helpful in differentiating chronic bacillary dysentery from chronic ulcerative colitis.

In 1934 Felsen and Osofsky [21] studied an epidemic of Sonne dysentery and found that the agglutination test was valuable in diagnosing mild and symptomless attacks and in detecting carriers. They found that arthritis is frequently associated with the Sonne bacillus infection.

The following year Felsen and Osofsky [22] reported some additional work on 300 control cases. By use of the agglutination test they discovered twenty cases of chronic bacillary dysentery which had been diagnosed as nonspecific ulcerative colitis; 23 per cent of their control group showed positive agglutinations.

Cases of acute and chronic bacillary dysentery were investigated by Felsen [23] in 1936. He found that long after the dysentery organisms disappear from the feces the intestinal lesions persist and the agglutination titer remains high. With Sonne dysentery, however, the titer may never have exceeded 1:50. Results of agglutination tests showed that many cases of nonspecific colitis had at first been bacillary dysentery.

In the same year Manson-Bahr [24] reported a careful study of the differential diagnosis of colon diseases. He found the agglutination test valuable in the chronic stages in order to differentiate it from colitis.

The clinical picture of this disease is bizarre. However, there is practically always a history of a previous acute diarrheal episode, which may have lasted from a few days to a few weeks. Then, for some unknown reason, periods of diarrhea recur from time to time and in some cases may even persist for months. If diarrhea persists long enough, the patient may show the usual signs of loss of weight and emaciation. Fecal examination of these persons may occasionally show some pus but rarely blood, unless there is an acute aspect to the condition. In a small percentage of examinations the etiologic organism may be recovered from the stool. Recently Silverman [25] of New Orleans devised a method of procuring more positive cultures from the stool by changing the intestinal flora from a proteolytic to an aciduric type.

Proctosigmoidoscopic examination, unless there is secondary infection, reveals no significant changes. The mucosa is blanched; the minute blood vessels stand out on the pale mucosa. Rarely, if ever, does one see ulcers; if they are present they are most likely small secondary lesions. Roentgenologically there are no pathognomonic signs. The haustral markings may be absent; there may be some tubalization of the descending colon and, in all cases, with barium enemas, not once was any unusual narrowing of the ileum noted similar to that found in regional ileocolitis. The most frequent complication of this disease is an arthritis, which may be monarticular in type, resembling an allergic joint, and as a complicating factor it was quite frequent in my group of cases. This is in agreement with the observations of Felsen.

Therefore the diagnosis of this condition must rest with the examination of the blood serum. A previous dysentery infection should be suspected in any patient who for some unknown reason has a persistent diarrhea that does not respond to ordinary methods of treatment after careful examination has ruled out the more common causes of diarrhea, particularly in view of the negative results on examination of the stool. Many patients date their trouble to the World War, and more recently there have been epidemics in Chicago resulting in subsequent outbreaks of paroxysmal diarrhea, which

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have been faultily ascribed to many other etiologic factors than are herein presented.

Seven years ago, after a careful search for the causes of persistent diarrhea, I found a high agglutinin titer for the various organisms of the dysentery group. Since then I have seen approximately ninety cases in which the blood serum gave a relatively high agglutination for one of the various organisms of this group. The interesting feature of this and subsequent studies, carried out at the Cook County Hospital, was that the Strong and Sonne bacilli were for the most part the causative organisms of the disease. Most laboratories in this community and elsewhere test for the Hiss Y, Shiga and Flexner bacilli and relatively few for the Strong and Sonne types. I am sure that this is the reason many cases remain undiagnosed.

In the technic followed, agglutinations in dilutions of 1:20, 1:40, 1:80, 1:160, 1:320, 1:640 and 1:1,280 were used, with a control tube for each. Each serum was run with Strong, Sonne, Shiga, Hiss Y and Flexner bacilli. Suspensions treated with solutions of formaldehyde, which are considered most reliable, were used and were tested at intervals of from one to two weeks for purity and agglutinability against known antiserums. All suspensions were made from smooth colonies. Sonne showed the greatest tendency to dissociate into rough variants and had to be transferred most often. Agglutinations were placed in an incubator at 35 C. (95 F.) for four hours and at room temperature for two hours before a reading was made. All readings were made with a magnifying lens.

From April 15 to Oct. 1, 1937, 237 cases of diarrhea were studied at the Cook County Hospital and 256 serial agglutinations were made, which consisted of the patient's serum tested against the Strong, Sonne, Shiga, Hiss Y and Flexner bacilli. In fifty-three of the 237 cases there were negative agglutinations (table 1). It might be said at the outset that agglutinations of 1:80 or above were considered diagnostic of a previous dysentery infection. Ninety-seven patients gave positive agglutinations of 1:80 and above for the Strong bacillus, twenty-six for Sonne, seven for Shiga, thirty for Hiss Y and sixteen for Flexner, making a total of 176 of these 237 patients positive for one of the various organisms of the dysentery group in dilutions of 1:80 or above. The Strong bacillus was by far the most prominent organism of the group to give a high titer of agglutinins.

Table 2 illustrates the studies of 144 patients selected at random who came to the hospital for other than diarrheal conditions. This group of cases was selected to see whether relatively high titers could be obtained in patients who had no recollection of a previous dysentery infection or who associated their diarrhea with an ordinary gastrointestinal upset. Of these 144 cases, twenty-nine were negative for all organisms and eighty-one gave a positive agglutination of 1:80 or above for the various organisms. These are further subdivided into forty-eight for Strong, eight for Sonne, seven for Shiga, nine for Hiss Y and nine for Flexner. In the diarrheal conditions the percentage of positive agglutinations in the blood was 79; in the control cases the percentage was 56. It is difficult in the control series to go into the history of all the patients because they were scattered throughout the hospital and many were in the outpatient clinic. However, it is reasonable to suppose that these eighty-one patients who gave a positive agglutination must have been exposed at some time or other to dysentery, if any credence is to be placed in the specificity of the agglutinations for these organisms. There is enough evidence in the literature and in the currently described work to support this contention.

As indicated in table 3, 133 of the patients with diarrhea had cultures of their stools made as a routine by the ordinary methods for obtaining positive dysenteric cultures; 111 of them gave negative reactions; twenty-two, or 16 per cent, gave positive reactions. Of the twenty-two, eleven, or 50 per cent, gave positive agglutinations for Strong; six, or 27 per cent, for Sonne, and five, or 22 per cent, for Flexner. No Shiga or Hiss Y bacilli were recovered in any of the positive stools.

Table 4 shows that from March 2, 1937, to April 1, 1938, 104 consecutive patients complaining of diarrhea were tested at my office. Forty-five of them gave positive agglutinations for one or more organisms of the dysentery group. Previously the agglutination tests had been done by outside laboratories, which accounts for the lack of control data for the other reported forty-five cases. Of the 104 patients who presented them-

TABLE 1.—*Patients Entering with a History of Diarrhea*

1. Diarrheas: 237 cases; 256 agglutinations; negative with all, 53

	Negative	1:20	1:40	1:80	1:160	1:320	1:640	1:1,280	Total 1:80 or Above
Strong	95	23	42	34	31	18	9	5	97
Sonne	175	24	35	16	8	2	0	0	26
Shiga	190	42	19	6	0	1	0	0	7
Hiss Y	189	17	18	16	9	3	1	1	30
Flexner	161	45	36	12	3	1	0	0	16
									176

TABLE 2.—*Controls*

2. Controls: 144 cases; 145 tests; negative with all, 29

	Negative	1:20	1:40	1:80	1:160	1:320	1:640	1:1,280	Total 1:80 or Above
Strong	51	16	34	28	13	5	2	0	48
Sonne	115	14	13	6	2	0	0	0	8
Shiga	114	18	11	6	0	1	0	0	7
Hiss Y	126	5	5	3	5	0	1	0	9
Flexner	102	18	21	6	3	0	0	0	9
									81

TABLE 3.—*Cultures*

Cultures Taken from 133 Patients	
Negative	111
Positive	22 (16 per cent)
Strong	11 (50 per cent)
Shiga	0
Sonne	6 (27 per cent)
Flexner	5 (22 per cent)
Hiss Y	0

TABLE 4.—*Office Patients with History of Diarrhea: Total 104 Patients*

Total positive, 45 cases

	1:20	1:40	1:80	1:160	1:320	1:640	1:1,280	Total 1:80 or Above
Strong	0	3	7	8	7	9	1	32
Sonne	1	0	1	2	0	1	0	4
Shiga	0	3	0	1	1	0	0	2
Hiss Y	0	1	6	7	3	0	0	16
Flexner	1	1	5	1	1	2	0	9
								63

selves for diarrhea, approximately 45 per cent had positive agglutinations. In table 4, thirty-two of these patients gave agglutinations of 1:80 or above for the Strong, four for the Sonne, two for the Shiga, sixteen for the Hiss Y and nine for the Flexner. Of these forty-five total positive cases, therefore, there were sixty-three agglutinations of 1:80 or above for the various organisms of the dysentery group. It is interesting to note that seventeen of the thirty-two agglutinations for the Strong type were 320 or above and that the others had correspondingly high titers.

COMMENT

Many patients complained of having had diarrhea for a period of years and gave negative results in the stool. The importance of making routine examinations of their serums is self evident. The data herein presented are suggestive that B. dysenteriae may infect a patient and later lead to recurrent diarrhea. The modus operandi of the clinical picture may be related to an allergic manifestation in which a sensitized intestine reacts to the antigen of the organism. The paroxysmal attack may resemble other bacterial allergic phases or it may resemble Shwartzman's phenomenon. The infrequency of the presence of the organism in the stool of the patient may suggest localization in the intestinal wall or, more logically, in the regional lymph glands. The cycle of the diarrhea is interdependent on the ability of the host to counteract the offending organism or its toxins. Further studies will have to be carried out to substantiate this point of view. The interesting feature is that, in a small group of control patients, after adequate therapeutic approach, the titer of agglutinins disappeared from the blood serum on subsequent examination. It should also prove enlightening to observe untreated patients during a quiescent period, to see whether the agglutinating titer remains as high or is absent when the diarrhea is in complete abeyance. This feature of the clinical picture is in the process of elaboration. I think it is justifiable to conclude that the bacillus of dysentery may infect a patient, the acute picture may subside and subsequent paroxysmal diarrhea may owe its origin to a previous infection based on the evidence of high agglutinating titer in the blood and in the absence of positive changes in the stool.

Except in relatively few cases, no attempt at a therapeutic regimen was carried out on any of the patients at the Cook County Hospital. However, those in my private service were subjected to the following therapy:

If the patient was critically ill, and occasionally he became so, he was hospitalized, placed on a high vitamin nonresidue diet and, if he showed no previous sensitizations, he was given a polyvalent antidysentery serum, beginning with 10 cc. the first day, 20 cc. the second day, 30 cc. the third day, 40 cc. the fourth day and 50 cc. on each of the fifth and sixth days. Following this program some serum sickness usually developed, which could be controlled by the ordinary methods. After the serum therapy the patient was given gradually increasing doses of a polyvalent or monovalent vaccine, depending on the specificity of the titer of the agglutinations in the blood. If the patient was ambulatory no serum was usually given, but he was started out immediately on a high vitamin nonresidue diet and given gradually increasing doses of the vaccine.

For specific treatment other than serum therapy, two types of stock vaccine were employed, one for oral and the other for hypodermic use. These were in polyvalent mixtures as well as in single strains. However, because of increased local and general toxic reactions, the Shiga organism was not used in the polyvalent mixtures. The oral vaccine contained 50 billion organisms per capsule; the hypodermic solution contained one billion organisms per cubic centimeter.

Patients receiving the oral vaccine took one capsule daily, half an hour before breakfast. If symptoms in the intestine were increased the dose was immediately reduced or the hypodermic vaccine given, since with the latter the dosage could be controlled more easily. With a decrease in symptoms in the intestine after from two to four weeks, the oral vaccine was given every second or third day and gradually decreased to one capsule weekly, provided the patient remained free from symptoms. The oral method was tried out because of the experience of some Russian investigators,[26] but in our hands it was not very effective.

The hypodermic vaccine was started at 0.1 cc. dose, subsequent doses being increased by that amount, unless a local or systemic reaction occurred, whereupon the dosage was either maintained or decreased. The schedule producing the best results is as follows:

Three injections a week for three weeks.
Two injections a week for three weeks.
One injection a week for six weeks.
One injection every two weeks for several months until the symptoms are in complete abeyance.

Variations, however, occur with the difference in the needs of the individual. In general the hypodermic vaccine gave better results.

The therapeutic results in these cases may be open to some question because one might possibly feel that one is dealing with nothing more than a reaction to a foreign protein injected into a patient. I have no proof to offer for the specificity of this form of treatment. Certainly further controls will have to be made in order to substantiate whether or not this is a specific reaction. I might say that in several of these cases, previous to the use of these vaccines, Bargen's vaccine filtrate and Bargen's immune serum gave no results in the few cases in which they were tried, and the patients did respond to the dysentery vaccine. Therefore I am merely offering this evidence as an observation on my part in order to be of some assistance in the treatment of these cases of unexplained diarrhea.

CONCLUSIONS

1. Recurrent diarrheas may be due to dysentery organisms.
2. Patients may become infected with bacillary dysentery organisms and later show agglutinins in the blood serum for the offending organism. These agglutinins remain for a long period of time.
3. Arthritis may be a complication of this form of dysentery.
4. In a relatively small number of cases the organism may be recovered from the stool.
5. Diarrhea associated with this phenomenon may be controlled by gradually increasing doses of monovalent and polyvalent vaccine given hypodermically.
6. In acutely prostrated individuals, monovalent and polyvalent antidysentery serum may be of value.
7. Further observations must be made before one can arrive at conclusions regarding the specificity of this form of treatment.

104 South Michigan Avenue.

26. Glukhoff, K. T., and others: Prophylak. med. 5: 64 (July-Aug.) 1926.

AIR CONDITIONING AND INDUSTRIAL HEALTH

LEVERETT D. BRISTOL, M.D., DR.P.H.
NEW YORK

The practical application of scientific air conditioning to various industrial processes and manufacturing methods and equipment first became evident about 1905. Air conditioning for human comfort was provided originally about 1922 in motion picture theaters and during the last ten or fifteen years has been made available with gratifying results in restaurants, stores, hotels, private homes, office buildings and railroad cars. Air conditioning may be defined as the mechanical production of an artificial indoor atmosphere through the simultaneous and complete control of temperature, humidity, movement and purity during various seasons of the year. While proper ventilation in general is recognized as one of the essentials for the maintenance of indoor life and health, little scientific information or statistical data are available as to the influence of complete air conditioning on the health of industrial workers.

AIR CONDITIONING SYSTEMS

There are various types of so-called air conditioning systems now in vogue. "Air conditioning" is a loosely used term which may mean one thing from the point of view of one person and an entirely different thing from the point of view of another; in fact, the words "air conditioning" and "air conditioned" are often misused. The popularity of the idea and the appeal to comfort, particularly the cooling effects in hot weather, already have given rise to a number of different devices now on the market. A true air conditioning system in the accepted use of the term is one that will provide simultaneously the exact indoor air temperature, moisture content, movement and purity required for a particular purpose, despite outside weather conditions; it must make available a complete rather than a partial conditioning.

As a rule a system designed to give simultaneous and complete air conditioning in a large building draws outside air to a centrally located conditioning apparatus in the building, where it is brought into contact with a dense water mist. The temperature of this water mist is automatically controlled either by heating or by cooling and in this manner the moisture content of the air passing through it is controlled. The water spray also serves as a filter to remove impurities such as dust particles and soluble matter. As the air leaves the spray chamber it may be heated or cooled to the desired degree of temperature according to the season of the year, and it is then carried through ducts and distributed to various rooms. In the winter months artificial heat and increased humidity are required, while during the hot and humid summer months the conditioning not only must cool the indoor air through some form of refrigeration but also must dehumidify it. In the conditioning process the volume of air circulated also is automatically regulated and controlled.

PREVIOUS STUDIES

One of the leading air conditioning companies has deplored the amazing lack of authoritative information regarding the effects of air conditioning on human health and has invited medical research and investigation on the subject; in spite of this, little controlled scientific data of value are available. Up to the present, most of the studies have been directed toward determinations of comfort effects, while a few comprehensive investigations on physiologic reactions have been carried on by various research workers representing such agencies as the American Society of Heating and Ventilating Engineers and the United States Public Health Service and Bureau of Mines.

SPECIAL STUDY

I had the opportunity to observe the results of air conditioning on the health of a particular group of industrial workers for a period of approximately three years. The system involved was one of the nationally recognized and approved complete air conditioning systems. The operating schedule of this air conditioning system was varied somewhat from time to time on a more or less experimental basis from the standpoints of comfort, effect on equipment, local weather conditions, season of the year, and current maintenance costs.

METHODS

In considering the possible effects of air conditioning on health, the difficulty in obtaining conclusive data must be recognized at the outset. Two approaches to a study of this nature are possible:

1. The positive approach, in which an attempt is made to measure the actual improvement in health and physiologic reactions based on careful periodic medical examinations, and studies of weight, nutrition, blood conditions, freedom from sickness and other factors relating to the positive health of each individual in the group.

2. The negative approach, in which an attempt is made to measure the amount, character and duration of sickness among members of an air conditioned group, as compared with a simultaneous control group not working in specially conditioned air.

In the study reported on, the positive approach would have involved considerable expense and a very close check-up on a large number of individuals, with possible disruption of routine service, as well as a hindrance caused by many variables which naturally would enter into such a study unless each individual in the group could be carefully controlled not only during hours of work but also during the entire twenty-four hours of each day. This investigation, therefore, is based on an analysis of the sickness experience of a group, compared with a suitable control group, as outlined under the negative approach mentioned.

GROUPS SELECTED

Approximately 1,000 female employees working in three or four air conditioned rooms in the same building were selected as the demonstration or study group, including only those having had at least two years of service at the beginning of the study and, so far as practicable, having had the same type of work during that time.

A control group of approximately the same number of women employees of about the same average age carrying on the same type of work in several other rooms of the same or nearby buildings under practically the same conditions, with the exception that they were working under ordinary conditions either of mechanical or of natural ventilation and not in so-called air conditioned space, was chosen for comparative study as to their sickness experience. The number of employees in each of the groups decreased somewhat and changed proportionately as the study progressed,

as the result of resignations, furloughs, change of place of work and other factors in connection with employment; therefore the sickness incidence rates, based on a slightly decreasing number of employees each month, have been computed and studied from the standpoint of number of cases per hundred employees.

STATISTICAL DATA

Two types of statistical data were available for this study, as follows: (*a*) those including cases of minor incidental sickness absence of seven days and less and (*b*) those based solely on cases of more serious illness lasting over seven days. Because of the fact that the number of cases of minor incidental absence of seven days and less may be subject to considerable distortion by unverified personal reasons for absence, and that many actual cases of brief illness may be recorded without a physician's diagnosis or certificate, it was decided to base this study on cases of sickness lasting more than seven days, all of which were reported and recorded on the basis of a physician's examination and diagnosis and were not liable to the influence of personal, employment and economic factors.

RESULTS

Table 1 gives a comparison of the average monthly incidence per hundred women employees of cases of sickness for periods lasting over seven days during thirty-three months of study in air conditioned and non-air conditioned groups.

TABLE 1.—*Comparison of Average Monthly Incidence Rates of Cases of Sickness During Thirty-Three Months of Study*

Group	Cases per 100 Employees	
	General Causes	Upper Respiratory Diseases
Air conditioned	1.62	0.72
Non-air conditioned	1.39	0.67

Table 2 gives a comparison of average days' duration per case of sickness for periods lasting over seven days, in air conditioned and non-air conditioned groups.

TABLE 2.—*Comparison of Average Days' Duration per Case of Sickness During Thirty-Three Months of Study*

Group	Average Days per Case	
	General Causes	Upper Respiratory Diseases
Air conditioned	41.5	29.7
Non-air conditioned	41.4	29.5

GENERAL COMMENTS

From this study there is no evidence to indicate any improvement in incidence or duration of sickness among a group of upward of 1,000 people working in scientifically controlled air conditioned space as compared with a control group of approximately the same size working in non-air conditioned quarters ventilated by the usual mechanical and natural methods.

The somewhat negative results in this comparative study may be based not so much on the lack of influence of air conditioning on absence because of sickness as on the satisfactory quality of the ventilation in this particular instance available to the control, non-air conditioned group. A study involving the comparison of scientific air conditioning with a wholly inadequate method or outworn system of ventilation obviously would show more definite results favorable to air conditioning in contributing to the reduction of the incidence and duration of sickness.

195 Broadway.

WEIL'S DISEASE

REPORT OF A CASE IN A FISH WORKER

SOLOMON GLOTZER, M.D.
BROOKLYN

The following case of leptospirosis icterohaemorrhagica (Weil's disease) is being reported because of its infrequency in this country and because of its possible implications with respect to its status as a compensable occupational disease.

REPORT OF CASE

J. S., a married white man, aged 33, a fish cutter, became ill Oct. 2, 1937. His previous history was negative and his family history was negative apart from the fact that his father has an inoperable carcinoma of the rectum. The present illness began with a sudden onset of chilly sensations, fever between 103 and 104 F., aches all over the body and a slight cough. He also complained of a severe frontal headache. The headache and generalized pains persisted for four days, accompanied by chilliness and a subsiding temperature, which reached normal on the fifth day. On the second day of illness he began to complain of abdominal cramping and nausea, followed by persistent vomiting. There was marked constipation and abdominal distention. Two days later a yellow discoloration of the sclera became apparent; the urine was dark and the stools were light.

The patient was first seen on the seventh day of illness, at which time examination revealed that he was acutely ill, almost moribund, stuporous and delirious and hiccuping continually. Jaundice was intense. Scratch marks and purpuric spots were visible all over the body. The conjuctivae were markedly injected. Deep scleral icterus was present, with a moderate degree of photophobia. The pupils were equal and regular and reacted to light. The ears and nose were normal, the tongue was coated and the pharynx was moderately congested. The gums were spongy and bled easily. Extensive hemorrhagic herpes labialis was present. Examination of the heart was essentially negative except for a bradycardia of 60 per minute. Wheezes and rhonchi were heard in the right lung posteriorly. The liver was palpable one fingerbreadth below the right costal margin and was tender; the spleen was not felt. The abdomen was distended, and spasm of the right upper rectus muscle was present.

October 9, the eighth day of illness, the patient on several occasions vomited a coffee ground material. The temperature was normal at this time. Dextrose was given parenterally. Two days later he was admitted to Kings County Hospital, where he remained only one day, refusing all treatment until he was taken home. At home the patient continued to vomit for two days more, and hiccuping continued until October 15. Dextrose was continued by mouth and intravenously, with insulin subcutaneously and liver extract intramuscularly. The patient began to improve, although a secondary rise in temperature began on the fourteenth day of illness and persisted for six days. October 23, the twenty-first day of illness, there was a recurrence of marked conjunctivitis in the left eye, which subsided after a few days. The patient made a complete recovery. The results of the laboratory examination of the blood are given in the accompanying table.

The urine October 11 contained albumin 1 plus, bile 4 plus, occasional granular casts and no leucine or tyrosine. Darkfield examinations of the urine for Leptospira were repeatedly negative.

Intraperitoneal inoculation of guinea pigs with urine on the fourteenth day failed to produce the characteristic disease in

these animals. Blood was sent to the Public Health Service in Washington, D. C., on the twentieth and thirty-eighth days of illness respectively, and both specimens showed positive agglutination in dilutions up to 1 in 30,000.

COMMENT

It is interestiing to note that this patient, when first seen, was considered to have acute yellow atrophy of the liver until examination of the blood revealed a severe azotemia. Since these observations could not be correlated with that diagnosis, Weil's disease was considered and confirmatory evidence was obtained. Further questioning of the patient elicited the fact that he worked in a fish market that was infested with rats which frequently came in contact with fish handled by him. In Aberdeen, a recent report [1] of the disease in forty fish workers calls attention to the great frequency of the disease in this occupation, to the extent that the diagnosis of "fish worker's disease" is often made by the patient. Transmission of the disease

Laboratory Observations of the Blood

	October 11	October 16	November 9
van den Bergh	Immediate positive	...	...
Sugar	106	...	...
Urea	180	72	...
Urea nitrogen	...	...	8.5
Creatinine	4.2	2.0	...
Cholesterol	...	310	...
Ester	...	210	...
Per cent of cholesterol as ester	...	68	...
Icteric index	150	86	19.2
Bilirubin	18 mg.	...	...

through the urine of infected rats has been proved by Ido [2] and later workers, who also examined the kidneys of rats in various parts of the world. In general it has been estimated that approximately 10 per cent of rats all over the world carry Leptospira in the tubules of the kidney without themselves showing symptoms, and excrete the organism in the urine. Infection in human beings usually occurs through breaks in the skin, but it has also been successfully demonstrated that, in guinea pigs, the disease may be reproduced by application of infected urine to the unbroken skin.[3]

Inada [4] divided the clinical courses of the disease into three stages:

1. The febrile stage lasts six or seven days and is initiated by a chill or high fever, accompanied by intestinal disturbances, headache, cramping muscular pains particularly in the gastrocnemius muscles, conjunctivitis and prostration. The urine contains albumin and casts. Cough, sore throat and vomiting are frequent. Hemorrhagic herpes labialis may occur. Leukocytosis between 10,000 and 20,000 and azotemia are usually present. Death rarely occurs during this stage. Leptospira is found in the blood at this time, so that inoculation of guinea pigs with blood will induce the typical reaction. It is not, as a rule, possible to demonstrate the organisms in the urine or to find antibodies in the blood during the first stage.

2. The stage of icterus begins on the seventh or eighth day and extends for five or six days. Jaundice, hemorrhagic tendencies, prostration, and nervousness and cardiac symptoms appear. Evidences of bleeding may be seen in all organs. Icterus occurs in only 60 per cent of cases. The liver is usually enlarged, the spleen only rarely. Azotemia becomes more marked, the blood urea ranging from 50 to 397 mg., and death from uremia may occur. The blood is free of organisms during this stage, but they can easily be found in the urine, where they may persist for forty days. The blood contains antibodies.

3. The convalescent stage begins on the thirteenth or fourteenth day. Improvement progresses with decrease in icterus and in the azotemia. Loss of hair occasionally occurs. Antibody production in the blood is complete; Leptospira is present in the urine, which may also contain antibodies. A secondary rise in temperature, the so-called after fever, occurs in from 28 to 40 per cent of the attacks, lasting from five to fourteen days, and may be accompanied by a secondary rise in blood urea as well.

The pathologic lesions involve primarily the liver, kidneys, skeletal muscles and capillaries. In the liver, proliferation and granular degeneration of hepatic cells, biliary stasis and periductal interstitial cellular infiltration are commonly found, with occasional areas of focal necrosis. The kidneys show swelling, granular degeneration and polyblastic invasion of the tubules and interstices, with subcapsular and interstitial hemorrhages. The skeletal muscles present punctate hemorrhages, hyaline degeneration and necrosis of the fibers. Vacuolization, loss of striations and infiltrations with cells are common. Capillary damage is indicated by minute hemorrhages, which occur in all tissues of the body.

Active immunization has been carried out in man, with an effect lasting from six to twelve months. Serum produced from horses and goats is being used therapeutically in Europe and Japan with good results if administered before the appearance of jaundice, but because of the infrequency of the disease in this country serum is not yet available here.

At the time this case was first seen, the American literature contained only twelve proved cases of Weil's disease. In the past few months, two further reports have appeared, bringing the total number of cases to twenty. This case is therefore the twenty-first to be reported in the United States and the second case found in a fish cutter. In view of the common incidence of the disease in fish workers in other countries, the question of its inclusion in the list of compensable diseases must be considered. That the disease is an occupational hazard cannot be denied, occurring as it does in all types of work in which the individual is exposed to contact with rat excreta. This question has already been raised in England. While it has not yet been declared compensable, a legal precedent was established there in 1925, when compensation was awarded for the death from Weil's disease of a coal worker, and the award upheld following an appeal (*Raeburn v. Lochgelly Iron and Coal Co., Ltd.*, 20 B. W. C. C., 637).[5] May 17, 1935, the widow of a sewer worker in England was awarded almost $3,000 for the death of her husband from this disease.[6] It is therefore apparent that the disease is an occupational hazard and, as such, individuals who have contracted the disease in the course of their occupation should be awarded compensation.

1. Davidson, L. S. P., and Smith, J.: Quart. J. Med. **5**: 263 (April) 1936.
2. Ido, Y.; Hoki, R.; Ito, H., and Wani, H.: J. Exper. Med. **26**: 341 (Sept.) 1917.
3. Inada, R., and others: J. Exper. Med. **23**: 377 (March) 1916.
4. Inada, R.: J. Exper. Med. **26**: 355 (Sept.) 1917.
5. Smith, H. E., communication to the editor: Brit. M. J. **1**: 39 (Jan. 5) 1935.
6. Compensation for Weil's Disease, editorial, Brit. M. J. **1**: 1081 (May 25) 1935.

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In New York City, as a harbor city, with its exposure to rat infestation, it is remarkable that many more cases have not been seen. It is possible that cases have occurred and have been overlooked. Our patient tells us of another individual working in the same market who has had jaundice recently. An extensive investigation should be pursued to determine the epidemiologic potentialities of the disease in this city, with an attempt at preventive measures.

SUMMARY

1. A case of leptospirosis icterohaemorrhagica occurred in a fish worker in New York City.

2. The question of its inclusion in the list of compensable diseases has been raised and precedents have been cited from the English courts.

3. The disease should be considered in the differential diagnosis of jaundice, especially in a waterfront city such as New York where rat infestation is present.

1684 West Second Street.

IDIOSYNCRASY TO PARALDEHYDE

JACOB KOTZ, M.D.
GEORGE B. ROTH, M.D.
AND
W. A. RYON, M.D.
WASHINGTON, D. C.

During the past few years many new methods have been introduced for the relief of pain during labor, their introduction being based on the belief (in which we concur) that analgesia and anesthesia should form just as necessary and as important a part in the proper management of obstetric cases as they do in surgical cases. However, any method used for the purpose must be carefully considered as to its relative efficiency and safety for both mother and child.

We have found that paraldehyde is an efficient obstetric analgesia-amnesia producing agent with a low toxicity and that when failures have occurred they have usually been due to insufficient dosage or improper technic. Toxic effects have rarely occurred, and these have appeared when the patient had an idiosyncrasy to the drug.

In the fatal case reported in this paper there was unusual susceptibility to paraldehyde. The hypersusceptibility was regarded as being probably produced by a pathologic condition in the patient, which was not discovered until necropsy, in this instance death occurring after 31 cc. of paraldehyde was given by rectum as a single dose in the beginning of labor.

Idiosyncrasy to drugs, a condition which may be defined as a susceptibility peculiar to the individual, usually consists in a hypersusceptibility in which (1) the ordinary action or (2) inconspicuous side actions of the drugs are greatly enhanced.

Many theories have been advanced to explain each form of idiosyncrasy, but as yet not one of them can be said to be universally accepted. The one which is probably regarded by pharmacologists as the most tenable is that idiosyncrasy is due to chemico-anatomic differences in certain organs of the sensitive person which, when the structures are acted on by drugs, give rise to abnormal functions.

From the George Washington University School of Medicine and Sibley Hospital.

TOXICOLOGY OF PARALDEHYDE

Before presenting the history of our case and the conditions found at necropsy, we shall discuss briefly the toxicologic aspects of paraldehyde in order to show that the dose used in our case would not have been excessive under ordinary conditions.

Toxicologists, pharmacologists and clinicians who have used the drug for sedation other than as a soporific consider paraldehyde to be a relatively nontoxic substance.

Underhill [1] stated that the toxicity of paraldehyde is low, that poisoning is rare and that the taking of as much as 100 Gm.[2] has been followed by recovery.

Leschke [3] searched the literature and could find only a few fatal cases of poisoning with paraldehyde. In one case, death followed the ingestion of 25 Gm., in another 52 Gm., the first apparently being the O'Brien case, in which death occurred four hours after the administration of from 22.5 to 26 cc. when the patient was delirious with typhoid. He further states that patients have recovered from as much as 150 Gm. Leschke reports a case in which recovery occurred promptly after 30 Gm. of paraldehyde, 3.2 Gm. of cyclohexenyl ethyl barbituric acid (phanodorn) and 0.4 Gm. of morphine.

Sollmann,[4] like other pharmacologists, states that the toxicity of paraldehyde is low and that 100 Gm. produced only very prolonged sleep. He considers that as a hypnotic in severe cases of insomnia the dose may be raised to 5-15 cc.

Cushny [5] apparently considered that the fatal poisonings reported in the literature were not altogether due to paraldehyde and hence stated that "very large quantities have been taken without fatal results and in fact without any more serious consequences than prolonged unconsciousness."

Dixon and Smart [6] regard paraldehyde as "one of the safest of the basal hypnotics, for there is no respiratory depression." They advise 1 drachm (4 cc.) doses hourly up to 1 ounce (30 cc.), if needed, in asthma and lobar pneumonia.

Webster [7] concludes that "the fatal dose of paraldehyde is difficult to state, as very large quantities have been taken without any serious consequences other than prolonged unconsciousness." He further cites the two cases referred to by Peterson and Haines.

Solis-Cohen and Githens [8] regard 20 cc. as not a dangerous dose in man and in support refer to the case reported by Mackenkie in which recovery followed the ingestion of 100 cc., the sleep lasting thirty-four hours.

Meyer and Gottlieb [9] regard paraldehyde "as a hypnotic which is really free from subsidiary actions on the functions of other organs." They advise from 4 to 6 Gm. in severe insomnia and state that from 30 to 60 Gm. has been taken without harm.

1. Underhill, F. P.: Toxicology, revised by Theodore Koppanyi, ed. 3, Philadelphia, P. Blakiston's Son & Co., 1936, p. 233.

2. Paraldehyde is a liquid, and since its specific gravity is 0.99 at 25 C., the dosage may be expressed either in grams or in cubic centimeters.

3. Leschke, Erich: Clinical Toxicology, translated by C. P. Stewart, Baltimore, William Wood & Co., 1934, p. 185.

4. Sollmann, Torald: Manual of Pharmacology, ed. 5, Philadelphia, W. B. Saunders Company, 1936, p. 731.

5. Cushny, A. R.: Pharmacology and Therapeutics, revised by C. W. Edmunds and J. A. Gunn, ed. 11, Philadelphia, Lea & Febiger, 1936, p. 363.

6. Dixon, W. E.: Manual of Pharmacology, revised by W. A. M. Smart, ed. 8, New York, Edward Arnold & Co., 1936, p. 44.

7. Webster, R. W.: Legal Medicine and Toxicology, Philadelphia, W. B. Saunders Company, 1930, p. 751.

8. Solis-Cohen, Solomon, and Githens, T. S.: Pharmacotherapeutics, New York, D. Appleton & Co., 1928, p. 1611.

9. Meyer, H., and Gottlieb, R.: Experimental Pharmacology, ed. 2, English translation by V. E. Henderson, Philadelphia, J. B. Lippincott Company, 1926, p. 105.

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Brundage [10] was unable to find a report of a fatal case but states that 1 drachm has produced serious symptoms and that recovery has followed a dose of 3½ ounces (105 cc.).

Heffter [11] states that the toxicity of paraldehyde in man is low, doses of from 10 to 12 Gm. producing only deep sleep with practically unaltered blood pressure and respiration.

Witthaus [12] does not list paraldehyde in his comprehensive work on toxicology, a remarkable fact when one considers that the drug had been employed since 1882.

Peterson [13] and Haines found "acute poisoning with paraldehyde very rare." They cite the O'Brien case in which death occurred in a patient with typhoid after a dose of about 25 cc., and that of Mackenkie, in which recovery occurred after 104 cc.

Clinicians have for some time been using paraldehyde as a preanesthetic agent. Stewart [14] used it in more than 500 cases rectally before operation, the adult dose being 30 cc. except when the patient's weight was less than 112 pounds (51 Kg.), when he used 1 drachm for each 14 pounds (6.4 Kg.) of weight. He has had no bad results.

Sourasky [15] employs paraldehyde by rectum in children as a preliminary to tonsillectomy, the dose being 1 drachm for each 14 pounds of body weight.

Garrett and Gutteridge [16] use paraldehyde as a basal narcotic, the rectal dose being 0.25 cc. per kilogram of body weight; that is, a man weighing 150 pounds (70 Kg.) would receive about 19 cc.

Kane and Roth [17] successfully use it rectally for the relief of labor pains, the dose being 1.2 cc. for each 10 pounds (4.5 Kg.) of body weight.

Kotz and Katzman [18] use it for obstetric basal analgesia, the dose being from 6 to 8 drachms (24 to 32 cc.), depending on the weight of the person and on the severity of the pains.

Rosenfield and Davidoff [19] use it for obstetric analgesia, giving from 4 to 6 drachms (16 to 24 cc.) by rectum in a single dose.

Colvin and Bartholomew [20] also use it as a basic amnesia producing agent in obstetrics, the rectal dose being from 6 to 8 drachms.

Fitzwilliams [21] considers it useful as a basal preanesthetic agent if the dosage is not greater than 1 drachm for each 14 pounds (1 stone) when given rectally in three equally divided doses over a forty minute period.

Henderson [22] uses it for producing preanesthetic narcosis, the average dose being from 20 to 25 cc. by rectum. He has given up to 100 cc. without untoward effects.

Piker and Cohn [23] use from 11 to 15 cc. one to three times daily for sedation in the management of delirium tremens.

Mackenkie [24] reported a case of a married woman who took 3½ ounces of paraldehyde; consciousness returned in thirty-one hours, recovery of ability to reply to questions in forty-one hours and complete recovery soon after.

MacFall [25] reported a fatality in a man aged 41 who had been accustomed to taking from 1 to 2 drachms of paraldehyde daily for some months. He apparently took as much as from 2½ to 3 ounces (75 to 90 cc.) before retiring and was found dead the next morning. Autopsy revealed hyperemia of the stomach and upper portion of the intestine and congestion at the bases of the lungs. The liver, spleen and kidneys were normal.

Raimann [26] described two cases in each of which a 50 Gm. dose was taken without manifestation of other effects than profound depression for from fourteen to nineteen hours.

An anonymous writer [27] reported to the editor of the *Lancet* a fatal ending after administration of from 6 to 7 teaspoonfuls to a woman, aged 20, who was in violent delirium from typhoid for which slight hopes were being entertained of her recovery. This case is known in the literature as the O'Brien (Bridget) case. Death occurred after four hours.

Brown [28] reported a case of paraldehyde idiosyncrasy in a man aged 20, weighing 123 pounds (56 Kg.), in whom deep unconsciousness took place after a dose of 16 cc. The patient was rather anemic, having had a gastro-enterostomy one year previously. Recovery from the paraldehyde occurred within twenty-four hours. The prominent symptoms present were complete loss of reflexes, profound stupor, very little depression of blood pressure, rise of temperature to 102.4 F. and diminished respiratory exchange.

McDougall and Wyllie [29] recently reported fatal poisoning in a woman, aged 44, who died fifty hours after taking 4 ounces (120 cc.) of paraldehyde. Their patient had a mental disorder and had leaped from a window about nine months previously, producing severe cerebral concussion. An autopsy was obtained and softening of the right temporal lobe of the brain was found. The temperature on the second day rose to 105 F., indicating that infection may possibly have been a contributing factor in her death.

More [30] described a case in which recovery occurred after 2 ounces (60 cc.) had been taken. A man, aged 71, was admitted to the hospital Nov. 28, 1933, at 11 a. m. in a state of profound unconsciousness, the temperature being subnormal and the pulse 130. Conjunctival and pharyngeal reflexes were absent. It was later learned that the patient had taken, on November 27, 2 ounces of pure paraldehyde as a hypnotic. Under treatment with stimulants, the reflexes began to return at 7 p. m. on the day of admission and there was complete consciousness at 7 o'clock the following morning.

REPORT OF CASE

A white woman, aged 31, was first seen in September 1936, at which time her weight was 143 pounds (65 Kg.). Her body was well developed and well nourished and showed no gross

10. Brundage, A. H.: Manual of Toxicology, Brooklyn, H. Harrison Company, 1926, p. 190.
11. Heffter, A.: Handbuch der Experimentallen Pharmakologie, Berlin, Julius Springer, 1923, pp. 1, 433.
12. Witthaus, R. A., and Becker, T. C.: Medical Jurisprudence, Forensic Medicine and Toxicology, ed. 2, Baltimore, William Wood & Co., 1911.
13. Peterson, F.: Legal Medicine and Toxicology, Philadelphia, W. B. Saunders Company, 1904.
14. Stewart, J. D.: Brit. M. J. **2**: 1139 (Dec. 24) 1932.
15. Sourasky, M.: Brit. M. J. **2**: 993 (Dec. 13) 1930.
16. Garrett, E. B., and Gutteridge, Eric: M. J. Australia **2**: 46 (July 8) 1933.
17. Kane, H. F., and Roth, G. B.: The Relief of Labor Pains by the Use of Paraldehyde and Benzyl Alcohol, J. A. M. A. **107**: 1710 (Nov. 21) 1936.
18. Kotz, Jacob, and Katzman, Sollie: Anesth. & Analg. **16**: 301 (Nov.-Dec.) 1937.
19. Rosenfield, H. H., and Davidoff, R. B.: New England J. Med. **207**: 366 (Aug. 25) 1932.
20. Colvin, E. D., and Bartholomew, R. A.: The Advantages of Paraldehyde as a Basic Amnesic Agent in Obstetrics, J. A. M. A. **104**: 362 (Feb. 2) 1935.
21. Fitzwilliams, D. C. L.: Brit. M. J. **2**: 472 (Sept. 7) 1935.
22. Henderson, John: Ann. Surg. **103**: 46 (Jan.) 1936.
23. Piker, Philip, and Cohn, J. V.: The Comprehensive Management of Delirium Tremens, J. A. M. A. **108**: 345 (Jan. 30) 1937.
24. Mackenkie, T.: Brit. M. J. **2**: 1254, 1891.
25. MacFall, J. E. W.: Brit. M. J. **2**: 255 (Aug. 8) 1925
26. Raimann, E.: Wien. klin. Wchnschr. **12**: 609, 1899.
27. Lancet **2**: 423, 1890.
28. Brown, Gilbert: Brit. J. Anesth. **13**: 25 (Oct.) 1935.
29. McDougall, John, and Wyllie, A. M.: J. Ment. Sc. **78**: 374 (April) 1932.
30. More, William: Brit. M. J. **1**: 428 (March 10) 1934.

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abnormalities. The eyes and ears were normal. The teeth were in good condition and the tonsils had been removed. The nose showed some mild catarrhal drainage from the sinus spaces. There was no evidence of any cervical or other glandular enlargement. The thyroid appeared normal. The lungs were normal to tactile fremitus, percussion and auscultation. The heart was normal in shape, size and position, the sounds being regular and of good intensity. No murmurs could be heard. The blood pressure was normal. There was no vascular sclerosis. The liver, gallbladder and spleen were not palpable. There was no edema of the ankles. Hemoglobin was 80 per cent (Dare) at this time. The urine was normal.

The patient's parents are still living and in fairly good health. She had whooping cough and scarlet fever during childhood, from each of which she made a complete and uneventful recovery. She is said to have had "walking typhoid" at 14 years but since she was not particularly ill at that time no blood tests were made to confirm such a diagnosis. She had a severe attack of sinusitis and bronchitis eleven years before we saw her and made a complete recovery from the bronchitis. The sinus infection improved after a short period spent in Florida. X-ray examination of the lungs showed no evidence of tuberculosis. After her return from Florida the appendix was removed, from which operation she made a normal recovery. Exploration of the gallbladder and pelvis at the time revealed no abnormalities. Periodic attacks of her sinus infection during the last eight years led to an exploration of the antrums about four years before we saw her. Little or no inconvenience was caused by the sinus infection during the last two years. She suffered from dysmenorrhea and menorrhagia for about five years previous to her marriage, but pelvic examination at that time showed a slight retroversion and a mild cervical erosion. The menstrual abnormality was relieved by endocrine therapy, and cauterization of the cervix cleared the erosion.

The patient's last normal menstrual period began Aug. 17, 1936. She experienced some nausea in September, which continued periodically until December, when she was advised to discontinue her work as a nurse.

Examination of the urine and blood pressure at this time and subsequently during the pregnancy showed both to be normal. The hemoglobin was determined in February and found to be 70 per cent. Administration of a proprietary liver preparation caused an increase to 83 per cent, at which figure it remained during the rest of the pregnancy. Calcium compounds and a vitamin D concentrate were also given throughout the pregnancy. During the last month of pregnancy edema of the ankles was present at the end of the day, but examination of the urine revealed no abnormality. Throughout the last two weeks she complained of lack of energy, with considerable exhaustion toward evening.

The appearance of edema, varying periods of nausea, lack of energy and exhaustion led to a complete examination May 15. In view of the symptoms of toxemia it was considered best to induce labor on the morning of May 20, at which time quinine and castor oil were administered. She was admitted to the hospital at 3 p. m. in active labor. At this time the blood pressure was 148 systolic, 98 diastolic and both maternal and fetal heart sounds were normal. Pelvic examination at 5:30 p. m. showed the cervix to be dilated 2.5 cm. with the head presenting in the left occipito-anterior position and partially engaged. Uterine contractions were occurring at intervals of from two to five minutes, the pains being quite severe. Having previously found that she took ether poorly and that she was sensitive to drugs (acetylsalicylic acid, morphine and codeine causing extreme nausea and depression), we decided, with the patient's consent, to administer paraldehyde as an analgesia-producing agent and accordingly 31 cc. of paraldehyde was given by rectum at 6:30. Ten minutes later the patient was in deep sleep. At 6:45 the respiratory rate suddenly increased from 20 to 40 per minute and the heart rate from 90 to 120. At 7 o'clock the patient went into coma with cyanosis, labored and rapid respiration and rapid, irregular pulse. The fetal heart rate had increased from 112 to 150 per minute. Two ampules of coramine was administered. At 7:30 the respiration was less labored, cyanosis had disappeared and the pulse rate had slowed to 110. Her condition continued to improve somewhat except that the deep coma persisted. At this time the pupils remained fixed in partial dilatation, and the uterine contractions diminished. The fetal heart rate dropped to 140 per minute. Auscultation of the maternal heart showed no presence of valvular insufficiency.

At this time one of us (J. K.) was called in consultation and it was believed that her condition was not alarming and that she would probably sleep through the night and deliver without difficulty in the morning. At 10 o'clock her condition suddenly changed, the patient again becoming cyanotic, the respiration labored and irregular, and the pulse rapid, irregular and weak. Auscultation disclosed a loud blowing murmur over the area of the tricuspid valve, indicating failure of the right side of the heart. The blood pressure was 118 systolic, 58 diastolic. Coramine and oxygen were then administered, which relieved the cyanosis and labored respiration; the cardiac condition, however, showed no improvement. About 250 cc. of blood was then withdrawn to relieve the pressure on the right side of the heart, following which 100 cc. of 25 per cent dextrose was administered intravenously. Digifolin was also given intravenously but the pulse continued to become weaker and more irregular, and the tricuspid murmur grew louder and more harsh. Oxygen was continued, since cyanosis resulted if it was withheld. Two doses (a total of 6 mg.) of picrotoxin were given intravenously without benefit.

At this time the patient's condition appeared hopeless, as pulmonary edema was marked. A cesarean section was performed at 1:50 a. m. May 21 and a live female child was born whose condition was poor, several hours of oxygen-carbon dioxide administration being necessary for resuscitation. The patient did not require further anesthesia for the section, since coma was so deep that all reflexes were abolished. Efforts at resuscitation were continued during the operation aside from the drugs that were used to stimulate cardiac action and respiration. Intratracheal suction was employed to prevent the patient from drowning in her own secretions and to allow the entrance of oxygen. Despite all efforts, including stimulation of the sino-auricular node as recommended by Dr. A. S. Hyman, death occurred at 2:50.

NECROPSY

The significant observations made at necropsy by Dr. Oscar B. Hunter, pathologist of the Sibley Hospital, were as follows:

On section there was a considerable amount of superficial fat of a pale lemon yellow color evenly distributed. The musculature was well developed; the fibers presented a moderately coarse appearance, which was more or less normal. When the abdomen was opened the stomach was markedly ballooned with gas. The intestine contained a moderate amount of gas. The uterus presented a normal appearance of a full term uterus which had been emptied. There was definite calcification of the costal cartilages. On closer examination of the chest the anterior aspect appeared to be slightly flattened and the ribs were slightly angulated at the junction of the costal cartilages. There was no evidence of any other gross abnormality. The thoracic and abdominal viscera were normal in position and relation except for considerable dilatation of the right side of the heart. The patient was moderately dehydrated. The abdominal and thoracic tissues were moderately dry. There was a small amount of emphysematous bubbles, probably the result of artificial respiration.

The thyroid, stomach, intestine, gallbladder, pancreas, uterus and urinary bladder were normal.

The liver was soft and of a slate gray. The capsule of Glisson was smooth and glistening. The cut surface showed evidence of toxic hepatitis of long standing. There was some staining with bile. There was evidence of well defined cloudy swelling, granular degeneration and fatty infiltration. There was considerable engorgement of the sinusoids with possible focal necrosis in the region of the central veins. The connective tissue in the periportal spaces appeared to be slightly thickened. Sections through various portions of the liver revealed no evidence of thrombosis, infarcts or abscesses.

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The spleen was well developed, slightly enlarged and adherent to the undersurface of the diaphragm. It showed a few superficial notchings. The capsule was slightly thickened and there was some proliferation of the malpighian corpuscles. The pulp was fairly firm and cut with slightly increased resistance. There was a mild degree of splenic tumor present.

The left kidney was normal in position and relation and the vessels and ureter entered and left in a normal manner. It was normal in size and fairly soft and there were small remnants of fetal outlines present. The kidney cut without increased resistance and the perirenal tissues contained a marked amount of fat. The cortex was swollen and presented a white and somewhat granular appearance with swelling of the columns of Bertini. The capsule stripped very easily, leaving a somewhat congested surface. The picture presented was that typical of a toxic nephrosis of some standing. There was no evidence of pyelitis or any infectious process.

The right kidney was normal in position and relation and presented more or less the same picture as the left side. There was a marked degree of hydro-ureter and hydronephrosis. It cut without increased resistance and showed considerable congestion and some edema. The pelvis was slightly dilated and the cortex was swollen with marked congestion of the interlobular vessels. There were considerable swelling of the parenchyma and cloudy swelling changes in the epithelium.

The left adrenal gland was quite soft, somewhat enlarged and quite congested. The cortex was yellow and the medulla was filled with blood. There was no evidence of adenoma or other unusual pathologic change present.

The right gland was enlarged, congested and somewhat swollen. The medulla and cortex presented much the same picture as the opposite side. There was no evidence of adenomatous changes or other specific pathologic changes.

The right side of the heart was dilated and the left side contracted. The right side collapsed when the blood was removed. The heart did not appear to be enlarged and there was a moderate amount of fluid in the pericardium. The vessels entered and left in a normal manner. There were no adhesions between the visceral and the parietal pericardium. There was a moderate amount of superficial subpericardial fat, which was normal in distribution.

The right atrium was widely dilated. The walls were stretched. The chordae tendineae and pectinate muscles were well developed but definitely stretched. There was some subendocardial fibrosis in the region of the fossa ovalis but there was no endocarditis.

The tricuspid orifice of the right ventricle was widely dilated, admitting four fingers. The tricuspid valves were well formed. There was a slight amount of thickening of the inferior margin of the leaflets. The pectinate muscles were well developed and the chordae tendineae were fine and delicate. There was no special enlargement of these structures. The columnae carneae tore with slight ease. There was definite evidence of chronic toxic myocardosis but no evidence of endocarditis or valvular disease present.

The pulmonary semilunar valves were well defined. There was slight thickening of the inferior margin but no sagging of the commissures.

The left atrium was slightly dilated. There was some subendocardial fibrosis of a patchy character, for the most part in the region of the fossa ovalis. There was no evidence of endocarditis.

The mitral valves of the left ventricle were well defined. There was slight thickening of the inferior margin of the middle leaflet and some beginning sclerosis at the bases of the leaflets. The columnae carneae were well defined and the musculature was very pale. There was a small amount of chicken fat clot. There was evidence of definite toxic myocardosis.

The semilunar valves were well defined; there was slight thickening of the inferior margin but there was no sagging of the commissures. There was also slight thickening of the bases. There were some soft, punctate, early atheromatous spots. The aortic orifice was patent.

Transverse sections through the coronary showed no evidence of coronary thrombosis or occlusion. The cut surface exuded liquid blood.

The great vessels of the neck were normal in position and relation. The aorta was soft and pliable.

There was no evidence of enlarged lymph nodes in the mediastinum, peribronchial or peritracheal regions.

The left lung was free in the pleural cavity. There was no increased amount of fluid present. There was marked congestion of the lower lobe with some petechial hemorrhages under the visceral pleura of the posterolateral aspect. The upper lobe showed compensatory emphysema. There was considerable congestion posteriorly. There was no evidence of infarcts or abscesses. Sections through the bronchial tree showed a moderate amount of frothy fluid and considerable mucus but no evidence of any obstruction of the bronchi. There was marked hypostatic congestion of the lower lobe. There was very little air in the alveoli. The upper lobe showed much the same picture posteriorly with evidence of compensatory emphysema in the anterior aspect.

The right lung was free in the pleural cavity. There was marked hypostatic congestion of the posterior aspect of the lower lobe with numerous petechial hemorrhages, probably the result of artificial respiration. The lung was quite heavy and the bronchi were filled with a considerable amount of grayish mucus and frothy fluid. The upper lobe showed considerable hypostatic congestion and edema. The lower lobe was quite dark and markedly edematous and showed pronounced hypostatic congestion. There was no evidence of infarcts, abscesses or pneumonia.

The anatomic diagnosis was:

1. Toxemia of pregnancy.
   (*a*) Marked toxic hepatitis with cloudy swelling and fatty infiltration.
   (*b*) Toxic nephrosis with pronounced cloudy swelling and a mild degree of hydronephrosis and hydro-ureter, particularly on the right side.
2. Mild chronic splenic tumor with toxic hyperplasia of the malpighian corpuscles.
3. Toxic adrenalitis with marked congestion.
4. Toxic myocardosis with marked dilatation of the right side of the heart.
5. Marked hypostatic congestion and edema of both lungs.

COMMENT

Under paraldehyde analgesia certain pharmacologic changes occur that are recognized as being normal. The conjunctival and corneal reflexes are absent and the pupils contract. The blood pressure drops from 10 to 30 mm. of mercury, the pulse rate being increased from 20 to 70 beats per minute. The respiratory rate is increased from 4 to 10 per minute with increased amplitude. The patient is in deep sleep.

At the time during labor when one of the authors (J. K.) was called in consultation, our case presented this picture, although a somewhat exaggerated one. The abrupt change that occurred shortly thereafter indicated the onset of cardiac failure, from which the patient did not recover. This failure was shown at necropsy to have had a definite anatomic basis. Its onset was probably precipitated by the drug administered.

Since January 1935 we have used paraldehyde in more than 600 labor cases with very gratifying results. It is an effective analgesic which is relatively quite safe. We believe that its use should not be discontinued because of our one fatality incident to its administration, an event which might occur with any drug to which a patient is hypersusceptible. Such hypersusceptibility to paraldehyde seems to be quite rare. It is best, however, that the use of paraldehyde should be limited to hospital patients since the patient under its influence requires special care, particularly during labor.

1335 H Street N.W.—1140 North Capitol Street N.W.

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Clinical Notes, Suggestions and New Instruments

TOPHI OF THE HEELS

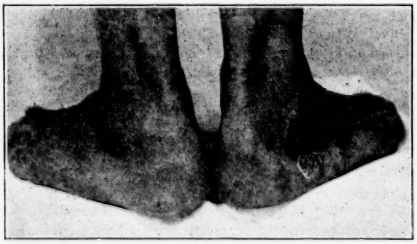
FREDERICK CHRISTOPHER, M.D.
Associate Professor of Surgery, Northwestern University Medical School; Chief Surgeon, Evanston Hospital
AND
STANLEY E. MONROE, M.D.
EVANSTON, ILL.

Gout is doubtless more prevalent than is commonly believed, yet the presence of tophi that simulate other lesions is quite rare. Out of a total of 24,766 admissions to the medical wards of the Peter Bent Brigham Hospital from 1913 to 1924 there were forty-four cases of gout.[1] In Hench's series of 100 cases from the Mayo Clinic, proved tophi were found in forty-one.

While tophi may be found in many locations, they have, according to Monroe,[2] a peculiar affinity for the ears. In this location he found them in 90 per cent of his cases. Tophi of the heels resembling pyogenic lesions are extremely uncommon.

REPORT OF CASE

B. H., a man aged 61, a blacksmith, came to our office in the fall of 1937 complaining of discharging lesions on the heels and pain in the heels associated with these sores. Examination of the heels revealed on each an indurated lesion about the size of a quarter (24 mm.). The lesions were slightly



Ulcerated tophi of the heels.

raised and not sharply delimited. Each was ulcerated in a small area near its center. From these small eroded centers a thick, gray, stringy material was obtained. The patient remarked about this discharge and stated that it was similar to that obtained from similar lesions on previous occasions.

Examination of this material under the microscope revealed the presence of many acicular crystals. They were variously disposed, some assuming a group arrangement not unlike the appearance of the ray fungus. When some of this material was shaken up in a test tube of water, nothing resembling sulfur bodies or cayenne pepper granules could be seen. Culture yielded no growth.

Past history told of many attacks of pain in the joints. The first attack was characterized by severe pain in the knee. The patient was then about 30 years of age. This bout of pain was of such severity as to cause him to stay in bed most of the time for three or four weeks. Nearly coincident with this attack he noticed a small gray nodule in the right ear, which had been present most of the time since. The attacks of pain in the joints recurred several times a year and varied in duration from a few days to a week or more. Most commonly the pain would start in a big toe, the ankles, knees and hands also being commonly involved, and sometimes pain was complained of under the heels. Exposure to cold is credited with bringing on many of the attacks.

The lesions on the heels appeared as pimples in 1929. They increased in size and at times were painful. They have been opened five times under the supposition that they were of pyogenic origin. Recurrences varied somewhat in location. In 1932 enlargements appeared on the hands; they have slowly progressed. The largest ones are situated adjacent to the metacarpophalangeal articulations. At times they have become swollen and tender. The patient has been a moderate user of beer, except during prohibition. He had never been on a diet until this fall. His father suffered from a similar ailment.

Smears of the discharge from lesions on the hands and heels showed acicular crystals characteristic of sodium mono-urate. Uric acid on the patient's blood showed a uric acid content of 6.31 mg. per hundred cubic centimeters.

Treatment consisted of a diet low in purines, tincture of colchicum, incision and drainage of the lesions on the heels. The response to treatment was satisfactory.

SUMMARY

In a case of gout in which there were ulcerated tophi of both heels, the lesions had five times previously been mistaken for ulcerations of pyogenic origin.

1. Pratt, J. H., in Cecil's Textbook of Medicine, ed. 3, Philadelphia, W. B. Saunders Company, 1934.
2. Monroe, R. T.: M. Clin. North America **18**: 999 (Jan.) 1935.

CONTINUOUS NASOPHARYNGEAL SUCTION IN THE TREATMENT OF BULBAR TYPE OF POLIOMYELITIS

O. WILLIAM ANDERSON, M.D., SEATTLE

In most epidemics of poliomyelitis a variable percentage of the patients have bulbar involvement. In some epidemics the majority of such cases are rapidly fatal, while in other outbreaks some of these patients make a satisfactory recovery if symtomatic treatment is adequate.

Usually a prominent feature in bulbar poliomyelitis is inability to swallow because of paralysis of the muscles of deglutition. As a result of this paralysis there is a constant stasis of mucous secretion in the pharynx, and the removal of this secretion is probably the most important measure in the care of the patient. When it is not possible to have a special nurse constantly with a patient who requires frequent aspiration, there is always danger of the patient drowning in his own secretions. But even in cases in which suction is frequent a grave hazard exists that small amounts of material may lead to an aspiration pneumonia, which is almost surely fatal. In the early stage of severe bulbar types the amount of secretion is often excessive, and the patients are too acutely ill and weak to lie on their sides or face down and still do well. It is at such a time that continuous removal of the buccal secretions is of paramount importance. When the secretions are allowed to gather in the pharynx, the patient becomes characteristically apprehensive and restless. To introduce a suction tube periodically aggravates seriously an already grave condition.

The following method removes these secretions continuously with little or no discomfort to the patient and has been found much more satisfactory than the customary periodic suction. A No. 10 to 16 French catheter is used, the diameter depending on the size of the patient's nasal passage. From twelve to fifteen holes are burned into the distal half inch of the catheter with a hot needle. The catheter is inserted in the nose and, with the tongue depressed, adjusted so that the tip can be seen lying at the base of the tongue. The catheter is then fastened in this position by adhesive strips at the nostril. With the foot of the bed elevated and the patient lying on his back, suction now will drain the most dependent region of the pharyngeal cavity. The perforations of the catheter are limited to the distal half inch, as already mentioned, so that no energy is wasted above the pharynx. When the openings are made on all sides of the catheter tip it becomes impossible for them all to be closed by mucous membrane, thus lessening irritation to the mucous membrane and insuring continuous suction. The catheter is now connected to a portable water suction apparatus attached to a faucet. It is important that a trap (a corked bottle with two inlets) be inserted in the line leading from the catheter to the faucet. This eliminates the danger of backflow

From the Municipal Contagious Disease Hospital, Chicago Board of Health.

to the patient, which might result from a sudden change in pressure. This apparatus can be used over a considerable time, and if alternate nostrils are used every twelve to twenty-four hours no trauma to the nose or throat should result.

Several other advantages of this method have been noted. When the continuous suction is instituted, the patient loses his anxiety and promptly falls off to sleep. Those in attendance can be at ease, knowing that the secretions are being taken care of. Although for the first day or two of the acute stage the patient may have to subsist on intravenous fluids, nasal gavage feedings should be started as soon as feasible. With the nasal suction in place, the gavage feeding is given through the other nostril. If the patient regurgitates the feeding, which is always a possibility, the suction will take up the regurgitated feeding before it can be aspirated. Also the patient can be made more comfortable by being given small amounts of water by mouth. This loosens the sticky mucus that forms in the mouth. As this flows back into the throat, it too is aspirated.

This technic would seem equally useful in other conditions in which the removal of secretions gathering in the throat is a menacing problem. Patients with postdiphtheritic paralysis and those in a prolonged state of coma, such as occurs in encephalitis and head injuries, should be favorable subjects for the method described. Even patients with tetanus who cannot swallow because of spasm of the throat muscles might be helped in this way.

1305 Fourth Avenue.

Special Article

THE CHEMISTRY OF VITAMIN D

CHARLES E. BILLS, PH.D.
EVANSVILLE, IND.

This article and others recently published or to be published comprise a new series on the present status of our knowledge of the vitamins. They have been prepared under the general auspices of the Council on Pharmacy and Chemistry and the Council on Foods. The opinions expressed are those of the authors and not necessarily the opinions of either council. Reprints are not available but the articles will be published later in book form.—ED.

Studies of recent years have shown beyond a doubt that there are several chemically distinct forms of vitamin D. Nevertheless, this vitamin is still spoken of in the singular, chiefly as a convenience and because its multiple nature was not recognized for about a decade after the first form was discovered. Custom limits the application of the term vitamin D to antirachitic sterol derivatives and to the unidentified antirachitic components of fish oils and other foods which are supposed to belong to this group.

Of the several forms of vitamin D which have been recognized to date, two are known to be of prime importance in medicine. These are activated ergosterol and activated 7-dehydro-cholesterol. Other forms undoubtedly contribute to the total antirachitic effectiveness of certain agents, and it may be that the importance of some is greater than now appears. But for practical purposes, one may consider that all antirachitic medicines and foods owe their peculiar property chiefly to either or both of the two forms mentioned.

Activated ergosterol comes to the physician in several types of products which he may not always recognize as essentially identical. Ergosterol, activated by exposure to ultraviolet rays and dissolved in an oil, is viosterol in oil. Similar solutions are known abroad under several other trade names. Activated ergosterol separated from the unimportant by-products of irradiation and crystallized comprises one form of vitamin D in the pure state. This is known to English and American chemists as calciferol. The Germans sometimes call it vitamin D_2. Since ergosterol is the principal sterol of yeast, and probably the only activatable one present, it follows that irradiated yeast owes its antirachitic action to its content of calciferol. When irradiated yeast is fed to cattle, the milk obtained is known as "metabolized" vitamin D milk. Since milk normally contains no important amount of vitamin D, the vitamin D of this special milk is essentially the calciferol which is transferred from the yeast. Thus the vitamin D of viosterol, irradiated yeast and yeast milk is one and the same; namely, calciferol.

Activated 7-dehydro-cholesterol has been identified, somewhat incompletely, as the form of vitamin D to which most other antirachitic agents owe their virtue. 7-Dehydro-cholesterol appears to be the principal activatable sterol, or provitamin, in cholesterol, the chief sterol of animal fats. Its active form thus comprises the vitamin D, which is produced in the skin, fur or feathers of animals exposed to sunlight or other sources of ultraviolet rays. For the same reason it is the form of vitamin D present in irradiated milk. It has been identified in certain fish oils and probably is the chief form, though certainly not the only form, of vitamin D that these oils contain. Since fish oils are almost universally used in poultry feeds, it appears that a substantial amount of this form of vitamin D finds its way into eggs, supplementing the supply produced by insolation of the feathers and skin of the birds. (Eggs are the only common food, except fish, naturally containing substantial amounts of vitamin D.) Fish oil concentrates are widely used to "vitaminize" milk, and the milk so treated is essentially the same as irradiated milk, but different from yeast milk, as regards the kind of vitamin D which it contains.

ACTIVATED ERGOSTEROL

Activated ergosterol is the form of vitamin D best known to the chemist.[1] Its parent substance, or provitamin, ergosterol, is the characteristic sterol of fungi. Ergosterol was first obtained from mushrooms by Braconnot in 1811. It was rediscovered by several nineteenth century chemists and was particularly studied by Tanret between 1879 and 1908. Tanret named it ergostérine because of its occurrence in ergot and its similarity to the cholestérine of Chevreul. It is now prepared from yeasts and molds, in which fungi it occurs in amounts up to 2 per cent of the dry weight, the quantity varying with the species and conditions of culture. Its origin is obscure, but seemingly it is related more closely to the metabolism of carbohydrates than to that of fats.

Ergosterol, $C_{28}H_{43}OH$, forms small colorless crystals usually containing some water of crystallization. The melting point varies with the water content, being 166° C. for the nearly anhydrous sterol. Polariscopic measurements show $[\alpha]^{20}_{5461} = -171°$ and $[\alpha]^{20}_{D} = -132°$ in chloroform. Three double bonds are present. The heat of combustion is 9,950 calories$_{15}$ per gram. Commercial ergosterol contains about 5 per cent of

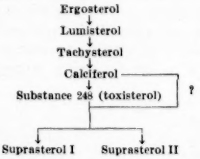
From the Research Laboratory, Mead Johnson & Co.

1. In this paper, most of the references are to recent studies. References to the earlier chemical and physiologic investigations are given in the author's previous reviews: Bills, C. E.: Physiology of the Sterols, Including Vitamin D, Physiol. Rev. **15**: 1-97 (Jan.) 1935; The Multiple Nature of Vitamin D, Cold Spring Harbor Symp. Quant. Biol. **3**: 328-340, 1935 (symposium of July 27); New Forms and Sources of Vitamin D, J. A. M. A. **108**: 13-15 (Jan. 2) 1937. Fieser, L. F.: Chemistry of Natural Products Related to Phenanthrene, New York, Reinhold Publishing Company, 1936.

α-dihydro-ergosterol, an inert sterol which always accompanies ergosterol in fungi and which is unaltered by irradiation. Ergosterol is insoluble in water, sparingly soluble in oils and freely soluble in most of the common organic solvents.

Although ergosterol is colorless, i. e., nonabsorbing of visible light, it absorbs certain ultraviolet wavelengths as powerfully as intense dyes do in the visible parts of the spectrum. It exhibits four narrow absorption bands, with maximums at wavelengths 260, 270, 282 and 293.5 millimicrons respectively. The phenomena of activation are closely associated with these bands of absorption.

When ergosterol is exposed to ultraviolet radiations of the wavelengths which it absorbs, a transformation into vitamin D (calciferol) begins at once. However, the ergosterol, even under the most favorable conditions, never gives a 100 per cent yield of calciferol. The transformation proceeds in overlapping steps, with the formation of a series of products of which calciferol is not the last. This intricate system has been studied most extensively by Windaus and his associates at Goettingen and can be illustrated conveniently, if not too well, by the following modification of a scheme given by Setz.



At no stage during the irradiation is any one of these substances present alone. More radiant energy seems to be required to decompose calciferol than to produce it, so that when the irradiation is not unduly prolonged calciferol is the chief product. Under the best conditions it may comprise nearly 50 per cent of the total, with tachysterol and lumisterol accounting for most of the remainder. Calciferol, lumisterol and the two suprasterols have been isolated in crystalline form. Tachysterol has been separated as a crystalline 3,5-dinitro-4-methyl benzoate. Substance 248, sometimes called toxisterol, has not been obtained pure.

The reactions are purely photochemical ones, little influenced by temperature. They can take place in boiling solvents or at room temperature or at the temperature of liquid air. Nothing is added to the ergosterol molecule and nothing leaves it. There is no polymerization. The changes are merely rearrangements within the molecule. Any wavelength of light that is absorbed by ergosterol can initiate the transformations. Activation takes place more effectively in solutions than in solid masses. Solutions that are agitated during irradiation are activated better than those which remain quiet. The presence of more than traces of air is detrimental. There is a specific solvent effect, in accordance with which various solvents which are satisfactory as to transparency and nonreactiveness are nevertheless unequally effective in promoting the activation of ergosterol dissolved in them.

To comprehend the molecular changes that occur when ergosterol and other D provitamins are irradiated, one must examine the structural formulas of these sterols. The accompanying figures and discussion are necessarily limited, though the field of sterol chemistry is wide.[1]

Figure 1 shows the accepted sterol ring structure, with a side chain as in ergosterol. The ring system is a phenanthrene-cyclopentane complex, the same as in many of the sex hormones. It is, incidentally, one of the biggest aromatic nuclei with which the animal body has to deal. Hydrocarbons of this type are formed when sterols are subjected to dehydrogenation with suitable reagents, such as selenium.

The prototype of all sterols is cholesterol, shown in figure 2. Ergosterol (fig. 3) differs from cholesterol in its side chain, which contains a double bond at C_{22} and a methyl group at C_{24}, and in its nucleus, which contains two double bonds instead of one. In hydroaromatic structures as complicated as the sterols, the possibilities of molecular rearrangement are great, yet most of those which are known to occur are *cis-trans* changes at C_3, C_5, C_9 or C_{10}. The spatial geometry of these changes is not perfectly understood, and structural formulas as ordinarily written do not show them.[2]

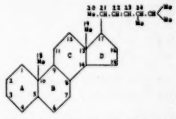


Fig. 1.—The sterol ring structure. Side chain shown as in ergosterol.

In all naturally occurring sterols (but not in the sterol derivatives called vitamin D), the hydroxyl group at C_3 is *cis* to the methyl group at C_{10}. It is a rule that this configuration exists when a sterol is capable of forming a precipitate with digitonin—the familiar analytical reaction by means of which cholesterol and ergosterol are determined. Since none of the irradiation products of ergosterol reacts with digitonin, it is assumed that in them the OH at C_3 is *trans* to the CH_3 at C_{10}. This rearrangement is probably the first change brought about by the activating rays and perhaps the only difference between ergosterol and lumisterol. Except for this difference, and the possibility of another steric difference at C_9, ergosterol and lumisterol are identical. Figure 3 is the formula for each of them, and also for pyro-calciferol and iso-pyro-calciferol, two sterols which result from heating calciferol. All four differ from one another only as *cis-trans* isomers, indistinguishable in ordinary, two-dimensional formulas.[2]

The change from lumisterol to tachysterol involves a deeper alteration of the molecule. The structural formula of tachysterol is not known with certainty, but since tachysterol and calciferol yield the same dihydro

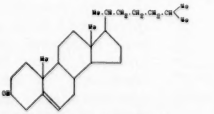


Fig. 2.—Cholesterol.

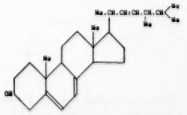


Fig. 3.—Ergosterol, lumisterol, pyro-calciferol and iso-pyro-calciferol.

derivative[3] the two must have the same carbon skeleton. Tachysterol, like calciferol which follows it, has four double bonds instead of the three exhibited by lumisterol and ergosterol. The fourth double bond arises by a rupture of ring B. Tachysterol was given

2. Schoenheimer, Rudolf, and Evans, E. A., Jr.: Allocholesterol and Epiallocholesterol, J. Biol. Chem. **114**: 567-582 (July) 1936. Windaus, Adolf, and Dimroth, K.: Die Konstitution des Lumisterins und der Erhitzungsprodukte des Vitamins D_3 (Calciferols), Ber. deutsche chem. Gesellsch. **70**: 376-379 (Feb.) 1937.

3. Müller, M.: Zur Kenntnis des Vitamin D und seiner thermischen und photochemischen Umwandlungsprodukte, Ztschr. f. physiol. Chem. **233**: 223-234 (June 7) 1935.

its name in recognition of the speed with which it enters certain reactions. A tentative structural formula, suggested by Lettré, is given in figure 4.

In the change from tachysterol to calciferol, the molecule returns to a relatively stable form. The formula may be written either as in figure 5, which emphasizes the relation of calciferol to the sterols (steroid formula), or as in figure 6, which emphasizes the broken

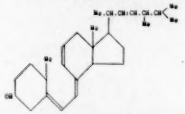


Fig. 4.—Tachysterol (a tentative formula).

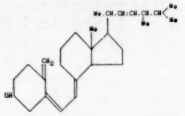


Fig. 5.—Calciferol (vitamin D_3). Usual, or steroid, formula.

ring B (stilbenoid formula). Different as the two formulas may look at first glance, they are actually the same. Figure 5 is the conventional representation, but figure 6 shows more clearly that the vitamin is not a sterol in the strictest sense, albeit a sterol derivative.

Irradiation of calciferol (i. e., overirradiation of ergosterol) occasions the formation of substance 248 and the two suprasterols. Substance 248 derives its name from its single intense absorption band, the maximum of which is at wavelength 248 millimicrons and is thus outstandingly different from the longer wavelength maximums of the irradiation products preceding it. Sometimes it is called toxisterol, in recognition of the toxic-calcifying properties which it exhibits out of all proportion to its antirachitic activity, if any. Toxisterol is formed most readily when alcohol is the solvent in which the overirradiation is conducted. When ether is the solvent it may not appear in detectable amounts. If it is formed at all it must immediately pass over to the suprasterols, into which it also passes when irradiation of alcoholic solutions is sufficiently prolonged. The substance has never been isolated, so practicaly nothing is known about it chemically.

The toxic properties peculiar to one particular brand of irradiated ergosterol solution were the subject of numerous reports in the medical literature of 1928 to 1930. The German manufacturer of the offending product had obtained two patents, one British [4] and the other American,[5] the specifications of which are most revealing. They call for the irradiation of ergosterol to be continued just until the absorption spectrum of what is now recognized as toxisterol attains its maximum! The mistake was clearly the result of assuming, in the absence of proper bio-assays, that the spectrographically most conspicuous irradiation product was the vitamin. That this is not so was known, even in 1928, from a study [6] conducted in this laboratory in which substance 248 was recognized as a decomposition product of the vitamin.

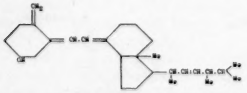


Fig. 6.—Calciferol, stilbenoid formula.

Whatever may be the number of double bonds in toxisterol, it appears that in suprasterol I the number is reduced from four to three. This results from a closure of the break in ring B, but the closure which in this case is brought about by prolonged exposure to ultraviolet rays is different from that which is produced when the two pyro-calciferols are made from calciferol by the action of heat. In suprasterol I the restored ring B may be five sided rather than six sided (fig. 7). Less is known of suprasterol II; the distinction I or II is arbitrary and does not indicate sequence of formation. Even the number of double bonds, to say nothing of their position, is unknown.[8]

In the accompanying table is a summary of properties of the irradiation products of ergosterol, including also the properties of the pyro-calciferols.

ACTIVATED 7-DEHYDRO-CHOLESTEROL

For several years after the activatability of ergosterol was known there prevailed a hypothesis, disproved by Waddell [7] in 1934, that traces of ergosterol comprised the provitamin to which the common sterols of animals and plants owed their activatability. This concept was based on the fact that the common sterols usually show the characteristic absorption spectrum of ergosterol more or less in proportion to their activatability. The possibility had been overlooked that there might exist other D provitamins having the same absorption spectrum as ergosterol.

On theoretical grounds it appeared that 7-dehydrocholesterol might be such a provitamin. This compound was prepared in the following semisynthesis by Windaus, Lettré and Schenck [8] and was found to be highly activatable. Cholesteryl acetate was oxidized by chromic acid to 7-keto-cholesteryl acetate. This was reduced by aluminum isopropylate to 7-hydroxy-cholesterol, the di-benzoate of which, when strongly heated, gave the mono-benzoate of 7-dehydro-cholesterol. From this the free sterol (fig. 8) was obtained by saponification.

Fig. 7.—Suprasterol I (a tentative formula).

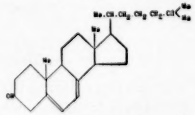


Fig. 8.—7-Dehydro-cholesterol.

In at least one instance, 7-dehydro-cholesterol has been chemically identified as the provitamin D of ordinary cholesterol. Windaus and Bock [9] isolated it from the sterol of hog skin. Boer, Reerink, van Wijk and van Niekerk [10] also isolated it from a crude cholesterol of unstated origin. However, ergosterol itself sometimes occurs in animal cholesterol, as was shown by Windaus and Stange [11] in eggs. This is probably an exceptional instance, associated with the fact that hens, unlike the mammals that have been investigated, absorb ergosterol from their food. The presence of ergosterol in eggs therefore seems casual, especially since the vitamin D of eggs is ordinarily not the ergosterol vitamin D, a form which, for birds, is relatively ineffective

4. British Patent 296,093, Nov. 15, 1928: Improvements in the Photochemical Production of Vitamin D from Ergosterol.

5. U. S. Patent 1,896,191, Feb. 7, 1933: Production of Vitamin D.

6. Bills, C. E.; Honeywell, E. M., and Cox, W. M., Jr.: Antiricketic Substances: IX. Quantitative Biophysical Studies on the Activation of Ergosterol, J. Biol. Chem. **80**: 557-563 (Dec.) 1928.

7. Waddell, J.: The Provitamin D of Cholesterol: I. The Antirachitic Efficacy of Irradiated Cholesterol, J. Biol. Chem. **105**: 711-739 (July) 1934.

8. Windaus, Adolf; Lettré, H. and Schenck, F.: Ueber das 7-Dehydro-Cholesterin, Ann. **520**: 98-106 (Sept.) 1935.

9. Windaus, Adolf, and Bock, F.: Ueber das Provitamin aus dem Sterin der Schweineschwarte, Ztschr. f. physiol. Chem. **245**: 168-170 (Jan. 29) 1937.

10. Boer, A. G.; Reerink, E. H.; van Wijk, A., and van Niekerk, J.: A Naturally Occurring Chicken Provitamin D, Proc. Acad. Sc. Amsterdam **39**: 622-632 (May) 1936.

11. Windaus, Adolf, and Stange, O.: Ueber das Provitamin des Eiersterins, Ztschr. f. physiol. Chem. **244**: 218-220 (Nov. 26) 1936.

in comparison with the vitamin D from 7-dehydrocholesterol.[12] The chief evidence that 7-dehydrocholesterol is the usual provitamin D of cholesterol is found in experiments with rats and chickens which show, in a word, that the vitamin D produced by irradiating the cholesterol from butter, brains, fish oils and other sources has the biologic properties of activated 7-dehydro-cholesterol rather than those of activated ergosterol.

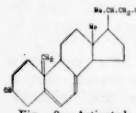


Fig. 9.—Activated 7-dehydrocholesterol (vitamin D_3).

Activated 7-dehydro-cholesterol, prepared by irradiating the synthetic provitamin, has recently been obtained in crystalline form by Schenck.[13] The crystalline vitamin has not yet been obtained from natural sources, but crystalline esters of it have been obtained from tuna[14] liver (species not specified) and halibut[15] liver oils. These esters resemble the corresponding esters of the artificially made vitamin, but the fish oil vitamin liberated from the esters could not be crystallized.

LESS IMPORTANT FORMS OF VITAMIN D

A provitamin D which is intermediate in structure between ergosterol and 7-dehydro-cholesterol was prepared by Windaus and Langer[16] by saturating the double bond in the side chain of ergosterol. Ergosteryl acetate was heated with maleic anhydride to form an addition product in which the two double bonds in ring B were saturated. The double bond at C_{22} was then hydrogenated, and the maleic anhydride was thermally split from the molecule, thus restoring the double unsaturation in ring B which is essential for activation. The free provitamin, known as 22-dihydro-ergosterol (fig. 10), was then obtained by saponification of the ester.

By exposure to ultraviolet rays, this is activated to the corresponding vitamin, which undoubtedly is 22-dihydro-calciferol (fig. 11). This product has been obtained in crystalline form by Windaus and Trautmann.[17] It has the same absorption spectrum as calciferol and demethyl-dihydro-calciferol. Its provitamin has the same absorption spectrum as that of the other two provitamins. It appears to be slightly less anti-

Physicochemical Properties of the Irradiation Products of Ergosterol and of the Thermal Decomposition Products of Calciferol

Substance	Melting Point, Degrees C.	Digitonin Reaction	Position* of Absorption Maximums, Millimicrons	Double Bonds	Specific Rotation, [α]D Rotation, Degrees	Solvent	Temperature, Degrees C.
Ergosterol	166	Positive	260, 270, **282**, 293.5	3	−132	Chloroform	20
Lumisterol	118	Negative	265, **280**	3	+192	Acetone	19
Tachysterol	?	Negative	268, **280**, 294	4	− 70	Benzine	18
Calciferol	116	Negative	265	4	+106	Alcohol	20
Toxisterol	?	Negative	248	?	?		
Suprasterol I	104	Negative	Only in far ultraviolet	3	− 76	Chloroform	18
Suprasterol II	110	Negative	Only in far ultraviolet	?	+ 63	Chloroform	19
Pyro-calciferol	95	Negative	274, **284**, 296	3	+502	Alcohol	20
Iso-pyro-calciferol	115	Partial	265, **280**, 294	3	+332	Chloroform	20

* The position of the most important band is indicated by the use of bold face type.

This fact, and also the fact that the potency appears to be significantly less than that of the crystalline vitamin, suggest that the vitamin preparations from fish oils were not pure, even though the evidence is good that they consisted chiefly of activated 7-dehydro-cholesterol.

The formula of activated 7-dehydro-cholesterol is shown in figure 9, from which its close relationship to calciferol (fig. 5) is evident. It is, in fact, a demethyl-dihydro-calciferol, just as its provitamin (fig. 8) is a demethyl-dihydro-ergosterol. Its absorption spectrum resembles that of calciferol, just as the absorption spectrum of its provitamin resembles that of ergosterol. Its antirachitic effectiveness is the same as that of calciferol for rats but many times greater for chickens.

In the German literature, activated 7-dehydro-cholesterol is called vitamin D_3. Calciferol is vitamin D_2. But there is no vitamin D_1, this term having been preempted for a lumisterol-calciferol mixture originally mistaken for the pure vitamin. Vitamin D_4 is the name applied to activated 22-dihydro-ergosterol, to be described.

rachitic for rats than the other two D vitamins, and for chickens its activity, per rat unit, is intermediate.[18]

22-Dihydro-calciferol, or vitamin D_4, has not been isolated from natural sources. Possibly its provitamin occurs in the phytosterols of the plant kingdom. If so, this form of vitamin D is produced when vegetable products are irradiated, and it may come to the interest of the physician in such forms as irradiated rolled oats and breakfast foods.

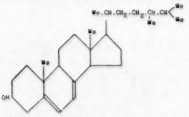


Fig. 10.—22-Dihydro-ergosterol.

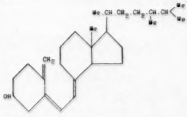


Fig. 11.—Activated 22-dihydro-ergosterol (22-dihydro-calciferol, or vitamin D_4).

By reactions analogous to those used in converting cholesterol into 7-dehydro-cholesterol, Wunderlich[19] has converted sitosterol (fig. 12) into 7-dehydro-sitosterol (fig. 13). This has the "ergosterol" absorption bands and can be activated to a vitamin, supposedly of the formula shown in figure 14. This vitamin, differing by a side chain ethyl group from activated 7-dehydro-

12. Bills, C. E.; Massengale, O. N.; Imboden, Miriam, and Hall, Helen: The Multiple Nature of the Vitamin D of Fish Oils, J. Nutrition **13**: 435-452 (April 10) 1937.

13. Schenck, F.: Ueber das kristallisierte Vitamin D_3, Naturwissenschaften **25**: 159 (March 5) 1937.

14. Brockmann, Hans: Die Isolierung des antirachitischen Vitamins aus Thunfischleberöl, Ztschr. f. physiol. Chem. **241**: 104-115 (July 2) 1936. Haslewood, G. A. D., and Drummond, J. C.: Antirachitic Substance from Tunny Liver Oil, Chem. and Ind. **55**: 598-599 (July 24) 1936. Simons, E. J. H., and Zucker, T. F.: An Antirachitic Substance from Tuna Liver Oil, J. Am. Chem. Soc. **58**: 2655 (Dec.) 1936.

15. Brockmann, Hans: Die Isolierung des antirachitischen Vitamins aus Heilbutt-leberöl, Ztschr. f. physiol. Chem. **245**: 96-102 (Jan. 29) 1937.

16. Windaus, Adolf, and Langer, R.: Ueber das 22-Dihydro-Ergosterin, Ann. **508**: 105-114 (Dec.) 1933.

17. Windaus, Adolf, and Trautmann, G.: Ueber das krystallisierte Vitamin D_4, Ztschr. f. physiol. Chem. **247**: 185-188 (June 15) 1937.

18. McDonald, F. G.: The Multiple Nature of Vitamin D: III. Irradiated 22-Dihydro-Ergosterol, J. Biol. Chem. **114**: lxv (May) 1936.

19. Wunderlich, W.: Ueber das 7-Dehydro-sitosterin, Ztschr. f. physiol. Chem. **241**: 116-124 (July 2) 1936.

cholesterol, appears to be much less antirachitic than the latter for rats. However, the two have not been compared in the pure state. Like vitamin D_4, this form of vitamin D may be produced when vegetable products are irradiated.

Again, by the same reactions, Linsert [20] has converted stigmasterol (fig. 15) into 7-dehydro-stigmasterol (fig. 16), which exhibits an absorption spectrum "very much like" that of ergosterol. Chemically, it differs from ergosterol only in that it has an ethyl group at C_{24}

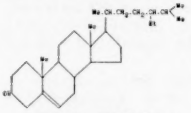


Fig. 12.—Sitosterol.

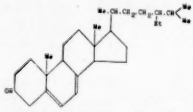


Fig. 13.—7-Dehydro-sitosterol.

instead of a methyl group. When irradiated, it most surprisingly does not become antirachitic, or at most very slightly so. This anomalous behavior, if true, is an instance of the fine specificity with which small molecular differences influence the physiologic properties of substances. It would be a matter of considerable theoretical interest to ascertain whether the reported failure of the expected new vitamin D is evident when the irradiated substance is given intravenously as well as when given by mouth.

Years ago, I observed that treatment of cholesterol with fullers' earth resulted in a slight activation. Yoder [21] has traced this reaction to the formation of cholesterilene, the probable formula of which (fig. 17) has recently been given by Stavely and Bergmann.[22] Cholesterilene sulfonic acid and its salts are definitely, though not powerfully, antirachitic for rats, and it has been reported that their effectiveness for chicks, per rat unit, is somewhat greater than that of cod liver oil. It will be observed that cholesterilene differs greatly in structure from the other forms of vitamin D.

Up to this point I have considered five forms of vitamin D, the chemical structures of which are well understood. Four of these are the active irradiation products of ergosterol, 7-dehydro-cholesterol, 22-dihydro-ergosterol and 7-dehydro-sitosterol respectively. The fifth, cholesterilene sulfonic acid, requires no irradiation. There are still other forms, as yet not understood chemically, but which deserve mention in passing.

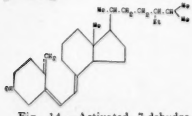


Fig. 14.—Activated 7-dehydro-sitosterol.

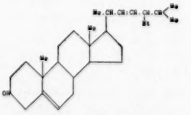


Fig. 15.—Stigmasterol.

Sixth: McDonald has found that by the irradiation of 7-hydroxy-cholesterol (or an impurity associated therewith) a slight antirachitic potency is developed. This may or may not be the same kind of vitamin D as that which is developed when cholesterol, freed from its normal provitamin and subsequently heated to produce a new provitamin, is irradiated.[1]

Seventh: Cholesterol freed from its normal provitamin but not heated to produce the new one gives on irradiation a vitamin D which is less effective for chickens, per rat unit than the vitamin D which is formed by irradiating either unpurified cholesterol or heat-treated purified cholesterol.[23]

Eighth: McDonald and I found that ergosterol, when suitably treated with nitrites, gives an active product of low potency. It is believed to be different from the ordinary forms of vitamin D which are destroyed by nitrites.[1]

Ninth: Weinhouse and Kharasch [24] have produced a form of vitamin D by irradiating the heated reaction product of 7-keto-cholesteryl acetate and isobutyl-magnesium bromide.

Tenth: Windaus and Trautmann,[17] in a footnote, mention "other provitamins, e. g., 22,23-oxido-ergosterol, which, however, are only feebly active after irradiation."

To correct a somewhat prevalent wrong impression, it may be pointed out that the kind of vitamin D which is produced by irradiating a given provitamin is not determined or even influenced by the conditions of irradiation. For example, from ergosterol, calciferol is the only kind of vitamin D produced. Whether long wavelength, short wavelength or mixed wavelength radiation is employed, as in different commercial processes, the end product is the same as regards the vitamin. The only differences are in the relative amounts of by-products, chiefly in the lumisterol and tachysterol, which are unimportant physiologically in the amounts present. Avoidance of the undesirable toxisterol is a matter of choice of solvent and duration of exposure.[1] Processes in which electron bombardment is substituted for ultraviolet irradiation produce the same kind of vitamin D, although they do so inefficiently because of extensive decomposition.[25]

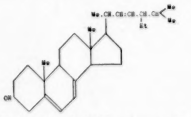


Fig. 16.—7-Dehydro-stigmasterol.

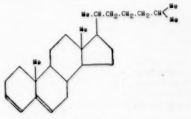


Fig. 17.—Cholesterilene.

Little has been said here with regard to the D vitamins of fish oils, which comprise by far the largest source of antirachitic medication for both man and animals. Demethyl-dihydro-calciferol (vitamin D_3), as already stated, appears to be the principal form of vitamin D present. However, the work of Bills, Massengale, Imboden and Hall [12] shows that more than one kind of vitamin D occurs in the liver oils of various species of fish. Even cod liver oil may contain a multiplicity of forms. Progress in separating and identifying the natural vitamins D may be expected from studies now under way in which the molecular distillation technic of Hickman [26] is applied to liver oils.

SUMMARY

The properties of vitamin D are exhibited by at least ten different sterol derivatives. Five of these are well understood chemically and five are distinguished by

20. Linsert, O.: Ueber das 7-Dehydro-Stigmasterin, Ztschr. f. physiol. Chem. **241**: 125-128 (July 2) 1936.
21. Yoder, L.: The Chemical Activation of Sterols: I. The Nature of the Floridin Activation of Cholesterol, J. Biol. Chem. **116**: 71-80 (Nov.) 1936.
22. Stavely, H. E., and Bergmann, W.: The Chemistry of Unsaturated Steroids: I. The Constitution of Cholesterilene, J. Org. Chem. **1**: 567-574 (Jan.) 1937.
23. Hathaway, M. L., and Lobb, D. E.: The Provitamin D of Heat-Treated Cholesterol, J. Biol. Chem. **113**: 105-110 (Feb.) 1936.
24. Weinhouse, S., and Kharasch, M. S.: Provitamin D Activity and Structure—Addition of Grignard Reagents to 7-Ketocholesteryl Acetate, J. Org. Chem. **1**: 490-495 (Nov.) 1936.
25. Hoffman, R. M., and Daniels, Farrington: The Formation of Vitamin D by Cathode Rays, J. Biol. Chem. **115**: 119-130 (Aug.) 1936.
26. Hickman, K. C. D.: Molecular Distillation: Apparatus and Methods, Indust. & Engin. Chem. **29**: 968-975 (Sept.) 1937.

fragmentary chemical and physiologic differences. The two that are of prime importance are the activation products of ergosterol and 7-dehydro-cholesterol respectively. A few of the others may have some practical significance, though most of them are merely of theoretical interest, illustrating the concept of the multiple nature of vitamin D.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT. HOWARD A. CARTER, Secretary.

OMEGA ELECTROLYSIS MACHINE NOT ACCEPTABLE

Manufacturer: Omega Electrolysis Company, 535 Fifth Avenue, New York.

The Omega Electrolysis apparatus, as the name implies, is designed to remove superfluous hair. It comes in both a portable and a cabinet model. Housed in a custom-built case, the portable unit weighs approximately ten pounds; the larger unit comes in a metal or wood cabinet as desired. Both models contain batteries as a source of energy.

Equipment includes shockproof holders for platinum needles and a support for them, so that a number of depilations may be performed at the same time. A metal cup is used as the indifferent electrode and is attached to the positive pole for operation. The portable model contains outlets for from six to eight needles; the larger models contain from eight to ten. One control lever (attached to the rheostat) and a meter are on the instrument panel. A dry battery, supplying approximately 9.2 volts, supplies current to operate the unit. The construction, underneath the instrument panel, is extremely simple, composed of a switch, meter, rheostat and terminals for the needles. Two bottles, one containing antiseptic and the other a sterilizing fluid, are part of the equipment. Neither of these preparations has been considered or accepted by the Council on Pharmacy and Chemistry.

Treatment procedure consists of inserting the needle into a hair follicle, following the direction of the hair, and applying sufficient current to dissolve the papilla, thus destroying the nutritive source at the root of the hair. This process takes from two to three minutes, depending on the strength of the current as well as the type of hair follicle particular to the individual.

A reliable investigator was appointed by the Council to report on the unit. He tried it out clinically. Although it worked satisfactorily when new, a question was raised as to its durability. A casual inspection of the makeup of the apparatus was convincing proof of the fragility of construction.

Even if it were made satisfactory mechanically, it still could not be acceptable because of the type of advertising matter circulated with it. This extols the merits of electrolysis, making the procedure appear to be very simple whereas in reality it should be attempted only by competent, trained physicians or specialists working under the supervision of a physician. The inexperienced operator is not apt to apply aseptic technic. As a consequence, infection and serious disfigurement may result.

The advertising matter is written to appeal to the beauty shop operator and the untrained technician. An "Omega Method" for becoming an expert "electrologist" is advertised, outlining the type of instruction given and offering a certificate to any one completing the course, either by home study or at the dealer's office. No evidence was presented to indicate that the instruction was given by qualified physicians trained in this branch of medicine.

The Council on Physical Therapy voted not to include the Omega Electrolysis machine in its list of accepted devices on the basis of an advertising policy detrimental to the public welfare.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

AMINOACETIC ACID (See New and Nonofficial Remedies, 1938, p. 51).

Aminoacetic Acid-Mallinckrodt.—A brand of aminoacetic acid-N. N. R.

Manufactured by Mallinckrodt Chemical Works, St. Louis.

ANAEROBIC ANTITOXIN (See New and Nonofficial Remedies, 1938, p. 383).

Mulford Biological Laboratories, Sharp & Dohme, Philadelphia and Baltimore.

Gas-Gangrene Antitoxin (Combined) Concentrated.—An antitoxic serum prepared by immunizing horses with the toxins of B. perfringens (Clostridium welchii) and Vibrion septique (Cl. oedematis maligni). After the desired potency is obtained, the horses are bled aseptically, the plasma is separated, and the antitoxin concentrated by a method which is similar to that used for concentrated diphtheria and tetanus antitoxin. The unitage is determined according to the method prescribed by the National Institute of Health. Marketed in packages of one syringe containing 10,000 units each of perfringens antitoxin and Vibrion septique antitoxin.

Dosage.—Therapeutic: The initial injection of the contents of one syringe preferably by the intravenous route, followed by the intramuscular or intravenous administration of repeated doses as indicated by the condition and symptoms of the patient.

Gas-Gangrene Antitoxin (Combined) Unconcentrated.—An antitoxic serum prepared by immunizing horses with the toxins of B. perfringens (Cl. welchii) and Vibrion septique (Cl. oedematis maligni). After the desired potency is obtained the horses are bled, and the serum is separated and prepared in a manner similar to other unconcentrated antibacterial and antitoxic serums. The unitage is determined according to the method prescribed by the National Institute of Health. Marketed in bottles containing 10,000 units each of perfringens antitoxin and Vibrion septique antitoxin.

Dosage.—Therapeutic: The initial injection of the contents of one bottle, preferably by the intravenous route, followed by the intramuscular or intravenous administration of repeated doses as indicated by the condition and symptoms of the patient.

POLLEN EXTRACTS-ABBOTT (See New and Nonofficial Remedies, 1938, p. 48).

The following dosage form has been accepted:

Mixed Grass Pollen Extract, Decimal Dilution Set: A mixture of equal parts of June grass, timothy, orchard grass, redtop, and sweet vernal grass pollen extracts, marketed in packages of five vials containing respectively, 5 cc. of a 1: 100,000 dilution (10 pollen units per cubic centimeter), 5 cc. of a 1: 10,000 dilution (100 pollen units per cubic centimeter), 5 cc. of a 1: 1,000 dilution (1000 pollen units per cubic centimeter), 5 cc. of a 1: 100 dilution (10,000 pollen units per cubic centimeter), and 0.5 cc. of a 3 per cent dilution (30,000 pollen units per cubic centimeter).

RHUS TOX. ANTIGEN-STRICKLER (See New and Nonofficial Remedies, 1938, p. 369).

The Mulford Colloidal Laboratories, Philadelphia.

Rhus Tox. Antigen-Strickler: Also marketed in packages of two 1 cc. syringes.

RHUS VENENATA ANTIGEN-STRICKLER (See New and Nonofficial Remedies, 1938, p. 369).

The Mulford Colloidal Laboratories, Philadelphia.

Rhus Venenata Antigen-Strickler: Also marketed in packages of two 1 cc. syringes.

VIOSTEROL IN OIL (See New and Nonofficial Remedies, 1938, p. 482).

Viosterol (A. R. P. I. Process) in Oil-Hospital Liquids, Inc.—A brand of viosterol in oil-N. N. R.

Manufactured by the American Research Products, Inc., a subsidiary of General Mills, Inc., Minneapolis, under license agreement with E. I. du Pont de Nemours & Co. U. S. patent applied for. (Hospital Liquids, Inc., distributor.)

Viosterol (A. R. P. I. Process) in oil (Hospital Liquids, Inc.) is prepared by the activation of purified ergosterol by low velocity electrons. The activated ergosterol is refined and dissolved in vegetable oil. The final product, when assayed according to U. S. P. method, has not less than the vitamin D potency of viosterol in oil-N. N. R.

DEXTROSE (See New and Nonofficial Remedies, 1938, p. 162).

Wm. S. Merrell Company, Cincinnati.

The following dosage form has been accepted:

Ampoules Solution Dextrose 50%, 100 cc.: Each ampule contains 100 cc. of a sterile aqueous solution containing 50 Gm. of dextrose-U. S. P.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, JUNE 25, 1938

TISSUE PREPAREDNESS FOR THE PRODUCTION OF SPECIFIC ANTIBODIES

In the past it has been presumed by some immunologists that the fixed tissues are autonomous in production of specific antibodies. Recent investigations indicate, however, that antibody production is further dependent on unknown hormonal or neurologic integrations.

Scores of unsuccessful attempts have been made to produce specific antibodies by adding antigens to tissue cultures. In spite of the few allegedly successful results the general consensus is that explants from the spleen, lungs and bone marrow of embryonic or adult laboratory animals are incapable of synthesizing precipitins, agglutinins, hemolysins, antitoxins or complement-deviating antibodies.[1]

Admitting these failures, recent investigators have modified the in vitro technic. They have injected antigens intravenously into experimental animals and after arbitrary intervals made tissue cultures from antigen-laden spleen or bone marrow. Landsteiner and Parker [2] of the Rockefeller Institute, for example, found that antigen-laden splenic fragments taken from rabbits injected from one to twenty-four hours previously with guinea pig erythrocytes failed to produce specific antibodies. If, however, an interval of from two to three days was allowed between the intravenous injection and the removal of the antigen-laden splenic fragment, agglutinins of relatively high titer were synthesized or secreted by the resulting tissue culture. Dr. Tsai [3] of the Microbiological Institute, Imperial University, Kyoto, reports a similar synthesis or secretion of diphtheria antitoxin in vitro by antigen-laden splenic tissues, removed from forty-eight hours to five days after intravenous injection of diphtheria toxin or toxoid.

Observations of this type seem to indicate that the production of antibodies by fixed tissues depends on certain wholly unknown preparatory reactions in the intact animal. These reactions are usually not completed until the second or third day after the intravenous injection of antigen. Landsteiner and Parker found that splenic fragments taken from animals given injections twenty-four hours previously, when cultivated in fully prepared serum, i. e., serum taken from control rabbits given injections three days previously, also fail to produce antibodies. From this they argue that serologic preparedness alone is insufficient; the splenic tissues themselves apparently must undergo a supplementary in vivo preparation.

These investigations seem to signify that production of specific antibodies can no longer be considered an autonomous function of fixed tissue cells but is rather a function of the body as a whole, working through local tissue preparedness for synthesis of antibodies. No one has yet attempted to formulate a theory as to the nature of this tissue preparedness, but knowledge of the nutritional, hormonal or neurologic factors involved may have important clinical applications.

1. Salle, A. J., and McOmie, W. A.: J. Immunol. **33**: 157 (Feb.) 1937.
2. Parker, R. C.: Science **85**: 292 (March 19) 1937.
3. Tsai, L. H.: J. Immunol. **33**: 471 (Dec.) 1937.

EPIDEMICS IN ENGLISH SCHOOLS

The great majority of English boys and girls receive their education in nonresidential schools; for this reason the maintenance of health in such schools is of preponderating practical importance. Twenty-one boys' schools and ten girls' schools agreed to participate in a statistical inquiry,[1] and investigation was begun in the Lent term of 1930. Although all large boarding schools cooperating are organized on the "house" system, the suggested uniformity of organization and environmental conditions does not actually exist. Great differences in house organization are found, especially in the boys' schools, while standards of accommodation vary not only between different schools but between different houses in the same school. These variations complicate epidemiologic questions to the extent that renders comparative discussion extremely difficult; nevertheless certain of the observations are definitely worth recording. The extensive study of nasopharyngeal infections and sore throats for example leads to the practical conclusion that, although an unusual incidence of sore throats should authorize vigilance with regard to the possible appearance of scarlet fever, otitis media or rheumatism, a low incidence of such infections is no guaranty of freedom from risk from these more serious diseases.

Knowing that the environmental conditions in girls' schools differ considerably from those of most boys' schools, the data from each were kept separately. It soon became obvious that the two populations, male and female, were being subjected to different influences which were reflected in the attack rates of nasopharyngeal infection. Such infections were much higher among the girls than among the boys, but, since the

1. Epidemics in Schools, Privy Council Medical Research Council Special Report Series, No. 227, London, 1938.

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records were limited to sickness causing at least one day's absence from school, two alternative explanations were possible: the girls may have been actually more susceptible to such infections or they may have been subjected to a stricter surveillance and on that account more likely to be kept out of school. It is perhaps not surprising that when the "common cold" and influenza were made into a single group of "nasopharyngeal infections" this group accounted for 53 per cent of all the time lost on this account among girls and for 43 per cent among boys. While it is possible that active methods of immunization against influenza may serve to cut the time lost from this cause, no promising method of immunization against colds has as yet become available.

Another interesting aspect of the report was that dealing with the relation between chickenpox and herpes zoster. Investigation showed that in eighteen out of twenty cases when zoster preceded chickenpox the first patient with chickenpox might, from the point of view of time, have been infected by a patient with zoster. When further examined, there seemed to be a suggestion that when zoster was the infecting agent the resulting attack rate of chickenpox was almost always small, whereas when chickenpox appeared first there was a greater chance of the disease spreading, although exceptions to both rules occurred. Evidence was not found, however, that chickenpox conferred immunity against zoster. The data on influenza showed (with the exception of one school) that there was no evidence of an actively acquired immunity lasting for as long as one year. In fact, in the pairs of epidemics analyzed, those who had influenza one year were more rather than less likely to contract it the following year in comparison with those who had escaped the first epidemic.

The examination of the record cards of the entire group at the beginning of the inquiry in 1930 showed that just over half the boys and just under half the girls had had their tonsils removed. These proportions rose slowly until, at the end of 1934, they had increased by almost 6 and 7 per cent respectively. The incidence of nasopharyngeal infections was studied in relation to this procedure. When the preoperative and postoperative history of the group of 364 boys whose tonsils were removed during school life were studied it was found that, whereas before tonsillectomy the attack rates from nasopharyngeal infection and time lost were appreciably higher than the average, after tonsillectomy these rates approximated closely the expected. Evidence was not obtained, however, that tonsillectomy resulted in a diminution in incidence of nasopharyngeal infections. The report concludes: "Though realizing the value of the operation in carefully selected cases, we have grave doubts as to whether the majority of tonsillectomies performed today are the result of true discrimination, rather than of routine ritual."

Although many other important epidemiologic problems are discussed, the report is careful to state that its main purpose is to formulate the epidemiologic problems needing study and solution rather than to draw extensive practical conclusions from a study which they still consider of a preliminary nature. Nevertheless the fund of information assembled can be considered a fundamental contribution to a subject of immense potential practical importance.

VITAMIN C AND COMPLEMENT

The factors governing the amount of complement in the blood of animals, especially the guinea pig, have long been obscure. Observations have been reported relating variations in complement to seasonal changes, disease and diet. Among these the last has received increasing attention; it has been suggested that vitamin C intake is of major importance in determining the complement titer. The evidence on this point, however, has not been conclusive. Recently Ecker and his associates [1] at Western Reserve University have reported extensive studies on the relation of vitamin C to complement. Many of the investigations on complement titer have been complicated by the difficulty of determining accurately the amount of this agent in a given sample of blood.[1a] In titrating complement, washed sheep erythrocytes and heated antiserum (obtained by injecting rabbits with sheep cells) are mixed, and the minimal amount of unheated guinea pig serum which must be added in order to cause complete hemolysis is determined. However, as several authors have indicated, it is impossible by this method to determine with any great degree of accuracy the amount of complement in guinea pig serum. Accordingly, Ecker and his collaborators used two methods of titration for their samples, one proposed by Koopman and Falker,[2] in which the minimal amount of serum necessary to initiate hemolysis is determined, and the other suggested by Brooks,[3] in which the amount of serum necessary to hemolyze 50 per cent of the erythrocytes is estimated. The amount of vitamin C in the blood was determined chemically.

Using these procedures, the Cleveland investigators showed a definite correlation between the amount of vitamin C in guinea pig serum and the complement titer.[1a] Animals on a scorbutigenic diet showed a diminution in amount of complement parallel with the decrease in vitamin C content of the serum. The

1. (*a*) Ecker, E. E.; Pillemer, L.; Wertheimer, D., and Gradis, H.: Ascorbic Acid and Complement Function, J. Immunol. **34**: 19 (Jan.) 1938. (*b*) Ecker, E. E.; Pillemer, L., and Wertheimer, D.: Complementing Activity and Ascorbic Acid Content of Guinea Pig Serums Following Ether Anesthesia, ibid., p. 39; (*c*) The Effect of Ascorbic Acid on the Constitution of Complement, ibid., p. 45. (*d*) Ecker, E. E.; Pillemer, L.; Martiensen, E. W., and Wertheimer, D.: Complement Activity as Influenced by Certain Chemical Agents, J. Biol. Chem. **123**: 351 (March) 1938; (*e*) Complement Function as Influenced by Szent-Györgyi's Hexoxidase, ibid., p. 359.

2. Koopman, J., and Falker, I. D.: More Sensitive Complement Fixation Test for Gonorrhea, J. Lab. & Clin. Med. **21**: 308 (Dec.) 1935.

3. Brooks, S. C.: Precise Titration of Complement, J. M. Research **41**: 399 (May) 1920.

feeding of ascorbic acid to scorbutic animals increased the complement titer. Similarly, the addition of crystalline vitamin C to serums deficient in complement increased the titer to normal and also rendered these serums more stable. The optimum level of vitamin C was found to be about 1 mg. in 100 cc. of serum. When the content of ascorbic acid was increased beyond this level no further effect developed on the complement activity. Ascorbic acid itself is not identical with complement, though it is essential to the activity of this factor in immunity. As Ecker and his collaborators found, crystalline vitamin C "will not hemolyze sensitized cells either by itself or in the presence of inactivated serum." [1a]

Complement that has been inactivated by certain procedures, such as prolonged shaking or treatment with ammonia, cannot be regenerated by addition of vitamin C.[1c] However, denaturation of complement by yeast or inactivation by aeration [1c] or by the addition of minute amounts of iodine, hydrogen peroxide or other substances [1d] may be reversed with ascorbic acid.

The mechanism whereby vitamin C affects complement function appears to be related to its reducing capacity. Glutathione, like ascorbic acid a physiologic reductant, appears also to be implicated in the reducing system affecting the complement activity of blood.[1e] Further, the Western Reserve investigators have found that inorganic reducing agents, such as hydrogen sulfide and sodium hydrosulfite ($Na_2S_2O_4$), can activate complement.[1d]

The fundamental work of Ecker and his collaborators has thus added an important chapter to knowledge of the biochemical basis of immune reactions.

Current Comment

PNEUMOCOCCUS POLYSACCHARIDE IN URINE

Urinary excretion of the specific capsular substances formed by pneumococci is of little or no diagnostic value, owing to the inconstant excretion of this substance during the early stages of lobar pneumonia. Cruickshank [1] of the University and Royal Infirmary, Glasgow, Scotland, however, believes that detection of the type-specific polysaccharide in the urine is a valuable prognostic index, the mortality among patients with "pneumococcosuria" being twenty times greater than that of pneumonia patients whose urine remains free from this polysaccharide during the course of the disease. Cruickshank's conclusions were drawn from his study of about 200 patients with pneumococcic infections, 184 of whom were suffering from lobar pneumonia. Type polysaccharides were estimated quantitatively in the urines of these patients by means of high titer type-specific antiserums. The serum used in most of his tests was capable of detecting homologous pneumococcus polysaccharide in dilutions as high as 1 : 5,000,000. The daily output of type pneumococcose in some of his cases was as high as from 3 to 30 mg. The mortality of his patients with type I or II polysaccharide excretion was about 40 per cent. The mortality among lobar pneumonia patients with polysaccharide-free urines was only 2 per cent. In a certain number of cases with delayed resolution the specific polysaccharide continued to be excreted for from twenty-five to forty days during convalescence, presumably as a result of the gradual dissociation of the pneumococcus hapten from its combination with humoral or intracellular antibodies. Whether or not urinary excretion of pneumococcus specific substances is a physiologic process or a pathologic process due to toxic injury to the kidney epithelium has not been determined. If, however, pneumococcosuria is a reliable prognostic index as Cruickshank believes, it may be a valuable guide to a rational therapy in lobar pneumonia. Cruickshank suggests that specific serum therapy should be limited to patients with positive pneumococcus polysaccharide in the urine.

1. Cruickshank, Robert: J. Path. & Bact. **46**: 67 (Jan.) 1938.

EFFECT OF CHILDHOOD ILLNESSES ON GROWTH

The opinion prevails that children who are frequently ill are "stunted" in their growth and unlikely to develop normally. The possible effects of recurrent illnesses on the physical growth of a group of normal boys and girls has now been investigated by Hardy.[1] The group was representative in socio-economic status, national origins and general intelligence of pupils in regular attendance in the public schools of an industrial urban community in the Middle West. The criteria of selection were principally dependent on the willingness of the parents to cooperate. Cumulative health histories were built up from information obtained in the home and records on file in the school office. Yearly interviews were held with the mother before the child was examined, and histories of the types and character of the illnesses were carefully checked. In general, the health histories obtained are believed to present a reasonably accurate account of all serious and prolonged illnesses during infancy and childhood. The types of illness included many of the rare as well as the ordinary childhood diseases. The incidence of illnesses during the first twelve years of life ranged from one to sixteen, exclusive of colds and rickets. The average number of illness episodes reported per child was six, with 13 per cent having had a history of nine or more illnesses and 14 per cent of three or fewer illnesses during infancy and childhood. Growth records were based on repeated measurements for eighteen physical traits on 218 boys and 197 girls from 7 to 12 or 13 years of age, taken without clothing by anthropometrists of the McCormick Fund. Final measurements also on 165 boys and 124 girls to 20 years of age were recorded. Evidence was not obtained of any general relation of illness histories to either rate of growth during middle and late childhood or size at maturity. The correlation gave no suggestion of any permanent deleterious effect of frequent sickness per se.

1. Hardy, Martha C.: Frequent Illness in Childhood, Physical Growth and Final Size, Am. J. Phys. Anthropol. **23**: 241 (Jan.-March) 1938.

FOURTH OF JULY INJURIES

Last year the American Medical Association resumed its annual summary of the injuries resulting from the celebration of the Fourth of July. In 1937 twenty deaths resulted from fireworks and firearms; two cases of tetanus occurred and there were 7,205 injuries. With the Fourth again imminent, unnecessary carnage already has begun to appear, one of the Chicago papers for June 16 carrying a report of a 7 year old boy who suffered severe burns of the face from placing a firecracker which he had found in the yard in his mouth to "smoke it." Again the cooperation of hospitals throughout the country has been requested to assist in carrying to the public consciousness the dangerous and unnecessary hazard of allowing fireworks to be sold indiscriminately.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Society News.—Dr. Samuel L. Ledbetter, Birmingham, discussed "Preoperative and Postoperative Treatment of Goiter" before the Calhoun County Medical Society in Anniston recently.——Dr. Edward C. Rosenow, Rochester, Minn., among others, addressed the annual meeting of the Alabama Dental Association in Birmingham, recently, on "Elective Localization of Streptococci and the Relationship of Dental Sepsis to General Health."——The Jefferson County Medical Society was addressed in Birmingham, recently, by Dr. Albert Graeme Mitchell, Cincinnati, on "Commonplace Endocrine Problems of Childhood." Dr. Hugh H. Young, Baltimore, discussed the removal of adrenal tumors before the society recently and Dr. Edgar W. Davis, Washington, D. C., on the scope of thoracic surgery.——Ernest C. Faust, Ph.D., professor of parasitology and member of the department of tropical medicine, Tulane University of Louisiana School of Medicine, New Orleans, gave the annual guest lecture of the Mobile Academy of Science, May 4, on "Malaria, with Special Reference to Its Epidemiology, Geographic Distribution and Prevalence in the Southern United States."

CALIFORNIA

Hospital News.—A bond issue was recently approved to finance the construction of a wing to the Palo Alto Hospital, on the campus of Stanford University. The new unit will provide eighty additional beds, doubling the present capacity of the hospital.

Personal.—Dr. Joseph M. Brown has been appointed health officer of Ferndale to succeed Dr. Oliver B. Barron and Harry W. Pasley of Reedley, succeeding Dr. Roy E. Allen.——The degree of doctor of laws was conferred on Dr. Jacob C. Geiger, director of public health of San Francisco, by the University of Santa Clara at its commencement June 4.

CONNECTICUT

Dr. Ross Harrison Retires.—Dr. Ross G. Harrison, since 1927 Sterling professor of biology, Yale University School of Medicine, New Haven, retired from active teaching at the end of the academic year. A dinner was held in his honor May 29 at the Osborn Zoological Laboratory, of which he is director. Born in Germantown, Pa., Jan. 13, 1870, Dr. Harrison received a degree of doctor of philosophy at Johns Hopkins University School of Medicine, Baltimore, in 1894, and a medical degree at the University of Bonn in 1899. He lectured in morphology at Bryn Mawr College, 1894-1895; taught anatomy at Johns Hopkins from 1896 to 1907, becoming in this year professor of comparative anatomy, a position he held until 1927 when he was appointed Sterling professor of biology at Yale. He has been managing editor of *The Journal of Experimental Zoology* since 1906. Societies of which he has been president include the American Society of Zoologists, 1924; American Association of Anatomists, 1912-1913; Anatomische Gesellschaft, 1934-1935, and the American Society of Naturalists. In 1914 he was awarded the Archduke Rainer medal of the Imperial Royal Zoological Botanical Society of Vienna. He has also been given the John Scott Medal and premium by the city of Philadelphia "for the invention of devices for tissue grafting and for tissue culture."

DELAWARE

Society News.—Dr. Francis C. Grant, Philadelphia, addressed the New Castle County Medical Society in Wilmington May 17 on "Diagnosis and Treatment of Spinal Cord Tumors." Dr. George Wilson, Philadelphia, discussed "Insulin in Mental Disease" at a meeting of the society April 19 and Dr. Richard Carmichael Tilghman, Baltimore, addressed the society recently on "Heart Disease in Pregnancy."

GEORGIA

New Superintendent at Hospital.—Dr. Ralph E. Porter, superintendent of the U. S. Marine Hospital, Fort Stanton, N. M., since 1934, has been appointed to a similar position at the marine hospital in Savannah. He succeeds Dr. Joseph S. Bolten who has been assigned to Washington. Dr. Porter has been associated with the U. S. Public Health Service since 1916.

Refresher Courses in Dentistry.—Walter C. McBride, D.D.S., Detroit, Mich., opened a series of refresher courses in children's dentistry under the auspices of the state department of health and the Georgia Dental Association. The following centers were selected for the lectures: Albany, May 23; Waycross, May 24; Swainsboro, May 25; Athens May 26, and Rome, May 27.

ILLINOIS

Spotted Fever.—Two cases of Rocky Mountain spotted fever have been reported in Marshall County thus far this year, one of which was fatal, newspapers reported June 15. The disease was first reported in Illinois in 1934. In 1935 there were five cases and six each in 1936 and 1937.

Chicago

Society News.—The Chicago Society of Allergy was addressed May 16 by Drs. Rudolph H. Hecht and Ben Z. Rappaport on "Infantile Eczema from the Viewpoint of the Allergist" and Tell Nelson, "Antigenicity of Horsehair."——The Chicago Roentgen Society was addressed May 12, among others, by Drs. Isador S. Trostler on "A Slipped Sacro-Iliac Joint" and Louis J. Tint, "X-Ray Findings in Sciatica."——At a meeting of the Chicago Ophthalmological Society, May 9, Drs. Harry W. Woodruff, Joliet, spoke on "Epithelial Corneal Graft for Recurrent Pterygium" and Agnes Beulah Cushman showed pictures of the International Congress of Ophthalmology at Cairo.——Dr. Melvin S. Henderson, Rochester, Minn., addressed the annual meeting of the Chicago Orthopaedic Society June 10 on "Use of Bone Grafts in Ununited Fractures of the Neck of the Femur" and Dr. Samuel Kleinberg, New York, "Slipping of the Femoral Capital Epiphysis."——A symposium on tuberculosis was presented before the German Medical Society of Chicago June 7 by Drs. Henry C. Sweany, Frederick Gruneck, George C. Turner and Richard M. Davison.

INDIANA

Personal.—Dr. Arthur W. Records has been appointed a member of the Franklin board of health to succeed the late Dr. Daniel R. Saunders.——Dr. James M. Hicks Jr., Huntington, has been appointed a member of the state board of medical examiners succeeding the late Dr. Leslie C. Sammons, Shelbyville. He will serve until 1941.——Dr. Henry F. Beckman, professor of obstetrics, Indiana University School of Medicine, Indianapolis, was presented with the annual award of merit of the Northwestern University Alumni Association in Indianapolis.

New Clinical Building at Medical School.—The new six story clinical building of the University of Indiana School of Medicine, Indianapolis, was dedicated May 14. The unit cost more than $600,000 and was partly financed by the PWA. The speakers at the dedicatory program included Dr. Dean Lewis, professor of surgery, Johns Hopkins University School of Medicine, Baltimore, whose subject was "Teaching the Medical Students How to Reduce the Cost of Medical Care"; Gov. M. Clifford Townsend; Herman B. Wells, A.M., president of

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Indiana University; William Lowe Bryan, LL.D., president emeritus, and Dr. Willis D. Gatch, dean of the medical school. Enlarged facilities for the treatment of cancer are a feature of the new building.

IOWA

Personal.—Dr. Russell R. Hansen has been appointed health officer of Storm Lake, succeeding Dr. Edgar F. Smith who recently resigned after holding the position for eight years.—— At a dinner held in honor of Dr. John H. Hovenden's completion of forty years of practice in Laurens, he was presented with a watch.——Dr. Charles V. Edwards, Council Bluffs, has been appointed assistant professor of obstetrics at Creighton University School of Medicine, Omaha.

Society News.—Dr. James H. Means, Boston, discussed "Medical Aspects of Preoperative and Postoperative Care" before the Linn County Medical Society, Cedar Rapids, May 26; Dr. Loyal Davis, Chicago, spoke on "Surgical Treatment of Peripheral Nerve Injuries" before the society recently.—— Dr. Samuel M. Feinberg, Chicago, discussed "Summer Allergy" before the Clinton County Medical Society at Clinton May 5. —— Drs. Harold J. McCoy spoke on "Hereditary Ocular Defects with Blindness" and Harry C. Willett, "Instability of the Neurovascular System as an Etiological Factor in Dermatosis" at a meeting of the Des Moines Academy of Medicine and the Polk County Medical Society recently.

LOUISIANA

Personal.—Dr. Theodore J. Dimitry, professor of ophthalmology, Louisiana State University Medical Center, New Orleans, has been appointed chairman of a monument committee to develop New Orleans as a city of monuments. It is planned to beautify the city's grounds with appropriate monuments, making Tulane Avenue the medical avenue of the city.——Dr. Edwin A. Socola has been promoted to clinical professor of pediatrics at Louisiana State University Medical Center, New Orleans, and Dr. Athol S. Kenney, assistant professor of pediatrics.

MARYLAND

Society News.—The Maryland Academy of Medicine and surgery was addressed in Baltimore recently by Drs. Edward A. Looper on "Diagnosis and Treatment of Infections of the Nasal Accessory Sinuses" and William H. Toulson, "Some Aspects of Genito-Urinary Tuberculosis."

Library Association's Lecture on Dentistry.—Dr. George G. O'Brien, assistant clinical professor of medicine, Loyola University School of Medicine, Chicago, delivered the second annual lecture of the Clarence F. Grieves Library Foundation of the Maryland State Dental Association recently in Baltimore; his subject was "Arthritis and Its Relation to Dentistry."

MASSACHUSETTS

Hospital Observes Twenty-Fifth Anniversary.—At a three day celebration May 5-7 the Peter Bent Brigham Hospital, Boston, observed its twenty-fifth anniversary in conjunction with a reunion of the graduates of the professional and nursing services of the hospital. The speakers included Gov. Charles F. Hurley; Mayor Maurice J. Tobin; Drs. Dean Lewis, Baltimore; Henry A. Christian, Elliott C. Cutler and Charles Sidney Burwell, Boston.

MICHIGAN

Meeting on Industrial Hygiene.—The Michigan Society of Industrial Hygiene held a dinner meeting at the Detroit-Leland Hotel, Detroit, May 25, and presented a symposium on the state, legal, engineering and medical aspects and current problems of industrial hygiene.

Hospital News.—A $160,000 building is nearing completion at Ypsilanti State Hospital for occupational therapy facilities. About 1,200 patients will benefit because 700 patients of the total at the hospital are now and will continue to be engaged in farming, carpentry, institutional laundering, housekeeping, kitchen work and grounds maintenance, it was stated.

Physician Mayors.—The following physicians have been elected mayors of the places indicated, according to the state medical society:

Dr. Thomas E. DeGurse, Marine City.
Dr. Frank V. Carney, St. Clair.
Dr. Arnold R. Miller, Harrisville.
Dr. Alden G. Sheets, Eaton Rapids.
Dr. Buell H. Van Leuven, Petoskey.

County Society Honors Past Presidents.—The Wayne County Medical Society honored its living past presidents at a meeting May 16 in Detroit. Keys containing miniature gavels wrought in gold were presented to the twenty-five living past presidents and a plaque was unveiled by Dr. Alexander W. Blain in memory of Dr. Arthur D. Holmes. Dr. Clarence E. Umphrey, the immediate past president, was given a silver tea service by the general membership.

Society News.—Dr. Clair Fremont Vale, Detroit, recently discussed "Cancer of the Stomach" before the Jackson County Medical Society, Jackson.—— The Genesee County Medical Society was addressed May 4 by Drs. Andrew C. Ivy and Latham A. Crandall Jr., both of Chicago, on "Clinical Aspect of the Physiology of the Gallbladder" and "Problem of Vitamins and Their Clinical Uses."——Dr. Michael L. Mason, Chicago, addressed the Muskegon County Medical Society in Muskegon May 22 on "Management of Open Wounds." Dr. Harold L. Morris, Detroit, addressed the society June 17 on "Pyelitis of Pregnancy."

MINNESOTA

State Medical Meeting at Duluth.—The eighty-fifth annual session of the Minnesota State Medical Association will be held at the Hotel Duluth, June 29-July 1. Dr. James M. Hayes, Minneapolis, will deliver the presidential address on "Medical Problems in Minnesota." Out-of-state speakers will include:

Dr. Irvin Abell, Louisville, Ky., Carcinoma of the Colon and Rectum.
Dr. Roland S. Cron, Milwaukee, Wis., Uterine Malignancy.
Dr. Howard W. Haggard, New Haven, Conn., Recent Advances in Medicine and Their Social Significance.
Dr. Philip Lewin, Chicago, The Foot and Ankle—Their Discomforts—Deformities and Disabilities.
Dr. Karl A. Meyer, Chicago, Recent Advances in the Treatment of Burns.
Dr. Eli K. Marshall Jr., Baltimore, Sulfanilamide in Bacterial Infections.
Dr. Charles Anderson Aldrich, Winnetka, Ill., Some Practical Points in the Management of Nephritic Children.
Dr. Edward Jackson, Denver, Recognition and Treatment of Refractive Errors in Children.

The first Herman M. Johnson Memorial Lectureship will be delivered Friday by Gov. Elmer A. Benson. Dr. Haggard will address the annual banquet Thursday evening; he will also address the public health meeting at the Orpheum Theater together with Dr. Abell. Dr. Hollis E. Potter, Chicago, will deliver the Russell D. Carman Memorial Lecture Wednesday afternoon on "The Diagnostic Roentgenology of Adult Pulmonary Tuberculosis with a New Suggestion as to Group Survey." The Southern Minnesota Medical Association will present its annual gold medal for the best scientific exhibit Thursday evening. The Minnesota Academy of Ophthalmology and Otolaryngology will hold a special dinner meeting at the Kitchi Gammi Club Friday in honor of Dr. Jackson who plans to give a course of lectures at St. Mary's Hospital, June 30-July 2, under the academy's auspices, on "Practical Aspects of Physiological Optics in Refraction." The annual golf tournament will be held Saturday morning at the Northland Country Club.

MISSISSIPPI

Health Officer Goes to Oklahoma.—Dr. John W. Shackelford, for eight years director of the Washington County health department, has resigned to become director of the technical field unit and serve as advisory officer for health units with the Oklahoma State Department of Health. He will begin his new work August 15, it was reported. Dr. Shackelford graduated at Tulane University of Louisiana School of Medicine, New Orleans, in 1926. He will be succeeded as county health officer by Dr. George W. Mast, Lexington, who now holds a similar position in Holmes County.

MISSOURI

Society News.—Dr. William W. Buckingham, Kansas City, discussed "Indications for Collapse Measures in Pulmonary Tuberculosis" before the Jackson County Medical Society May 24.——Dr. Hiram Winnett Orr, Lincoln, Neb., addressed the Buchanan County Medical Society in St. Joseph recently on "Prevention and Control of Infection in Injuries to Bones and Joints."——Dr. William A. Hudson, Detroit, addressed a joint meeting of the Trudeau Club of St. Louis and the St. Louis Medical Society recently on "Collapse Therapy—Its Principles and Application in the Treatment of Pulmonary Tuberculosis."——At a meeting of the Kansas City Society of Ophthalmology and Otolaryngology recently the speakers included Drs. De Forrest C. Jarvis, Barre, Vt., on "Value of 3-Unit Doses of Insulin in Ophthalmology and Otolaryngology" and "Applied Body Chemistry in Ophthalmology and

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Otolaryngology," and James W. White, New York, "Method of Checking Muscle Imbalance" and "Convergence Insufficiency with a Vertical Imbalance."

MONTANA

Personal.—Dr. Byron L. Pampel, Livingston, has been named superintendent of the state hospital at Warm Springs. ——Dr. Enoch M. Porter, Great Falls, was elected president of the state board of health at its recent meeting in Helena.

NEVADA

Plague Infection.—Plague infection has been found in fleas collected from Mohave Desert wood rats in Clark County: from rats trapped April 14, 14½ miles northwest of Las Vegas; from rats trapped April 18, 14 miles northwest of Las Vegas; from rats trapped April 19, 17 miles northwest of Las Vegas; from rats trapped April 20, 21 miles northwest of Las Vegas; from rats trapped April 21, 23 miles northwest of Las Vegas; from rats trapped April 22, 17 miles northwest of Las Vegas.

NEW JERSEY

Public Health Week.—The Bergen County Medical Society sponsored a public health week program May 7-14. The publication of a special medical section in the Bergen *Evening Record* opened the week's program. Other features included health movies, exhibits and lectures, and an x-ray clinic for Negroes. The section in the *Evening Record* contained sixteen pages of articles written by physicians and dentists, reproductions of pictures of members of the county medical society and advertisements.

Society News.—The Bergen County Council of Social Agencies sponsored a one day institute on welfare problems in Hackensack May 23.——At a meeting of the Essex County Medical Society in Newark recently, Dr. Thomas A. Shallow, Philadelphia, discussed "Carcinoma of the Thyroid Gland." ——Dr. John H. Gunter, Philadelphia, addressed the Gloucester County Medical Society on "Dental Problems of Interest to Physicians."——At a meeting of the Passaic County Medical Society in Passaic recently, Dr. S. Bernard Wortis, New York, read a paper by Dr. Foster Kennedy, New York, on "Allergy in Nervous and Mental Disease."——At the second annual meeting of the New Jersey Association of School Physicians in Atlantic City May 20 one session was devoted to a discussion of childhood tuberculosis with the following speakers: Drs. Berthold S. Pollak, Secaucus; Max Horn, Newark, and Irving L. Applebaum, Newark. Other speakers were Drs. Aaron H. Horland, Newark, on "The School Physician as the Representative of Organized Medicine in the Public Schools" and Harry B. Silver, Newark, "Our Relation to the State Medical Society."

NEW YORK

Consultants to Police Department.—A police scientific staff, composed of sixteen members, has been formed in Buffalo to serve as consultants to the local police. It is under the supervision of the police commissioner and five rooms are provided in police headquarters to house the ballistic, chemical and photographic laboratories and the rooms necessary for the polygraph. Meetings are held at regular intervals and all members are subject to call as the necessity arises. The following are members:

Dr. Charles W. Bethune, moulage expert.
C. Merrill Brown, M.A., microchemist.
Dr. John Burke, medical photographer.
Dr. William F. Burke, polygraph expert.
G. H. Cartledge, Ph.D., inorganic chemist and spectroscopic analysis.
Dr. Rocco N. De Dominicis, pathologist.
Dr. Karl F. Eschelman, firearms identification and ballistics.
Aaron A. Goldstein, librarian and secretary.
Dr. Charles E. Long, medical examiner.
William F. Payne, microscopic photography and x-ray.
Edward J. Powers, city chemist.
M. C. Rinhardt, M.A., physicist.
Clifford E. Rose, D.D.S., cryptography and dental identification.
Dr. Harry M. Steen, pathology and biochemistry.
A. P. Sy, Ph.D., toxicologist.
Dr. Victor A. Tyrasinski, police surgeon.

New York City

Dr. Cannon Delivers Welch Lectures.—Dr. Walter B. Cannon, George Higginson professor of physiology, Harvard University Medical School, Boston, delivered the William H. Welch Lectures at Mount Sinai Hospital in May; his subjects were "Some New Aspects of Homeostasis" and "The Aging of Homeostatic Mechanisms."

Appointments to New York Polyclinic.—The following have been appointed to the New York Polyclinic Medical School and Hospital:

Dr. Joseph F. McCarthy, professor of urology and attending urologist.
Dr. Charles J. Imperatori, professor of otolaryngology and attending otolaryngologist.
Dr. Joseph E. J. King, professor of neurosurgery and attending neurosurgeon.
Dr. Edward H. Dennen, professor of obstetrics and attending obstetrician.

Mosquito Eradication.—Under a recently approved WPA schedule, $2,540,000 will be expended for further control and eradication of mosquitoes and insect pests in the low lying sections of New York, especially Queens, it is reported. The major phase of the work will require the digging of ditches and the construction of retaining walls and dikes in swamps and ponds. According to the present plans 35 per cent of the operations will be done in the Queens sections, 20 per cent each for Brooklyn and Bronx low lying areas, 18 per cent in Staten Island and 7 per cent in Manhattan. In Queens the areas to be treated will include those surrounding the World's Fair grounds and others sections of Flushing, Howard Beach, Casino Park, South Aqueduct and south of Jamaica. In Brooklyn work will be done in the Casino and Bergen Beach sections; in the Bronx, the Pelham Bay marshy areas. In Staten Island, in Rosebank, Eltingville, Richmond Village, New Springville and Annadale.

Dr. Alger Wins Leslie Dana Medal.—Dr. Ellice M. Alger, professor of clinical ophthalmology, New York Post-Graduate Medical School and Hospital, has been awarded the Leslie Dana Gold Medal, given each year for "outstanding achievements in the prevention of blindness and the conservation of vision." Dr. Alger was selected for this honor by the Association for Research in Ophthalmology in cooperation with the St. Louis Society for the Blind, through which the medal is offered by Mr. Leslie Dana, St. Louis. Dr. Alger was one of the founders in 1915 of the National Society for the Prevention of Blindness and he has served continuously on its board of directors. The inscription on the 1938 medal refers to Dr. Alger as "A Pioneer in Sight Conservation—Wise, Understanding and Sympathetic Counsellor." Dr. Alger is 67 years of age and graduated at the University of Vermont College of Medicine, Burlington, in 1893. He formerly served as chairman of the Section on Ophthalmology of the New York Academy of Medicine.

Society News.—The New York State Society of Pathologists adopted its constitution and elected the following officers, among others, at a meeting May 10; Drs. William S. Thomas, president; Armin V. St. George, vice president, and Maxwell J. Fein, secretary treasurer. Committees were appointed to undertake to improve the economic situation of pathologists in the state.——The Bronx County Medical Society was addressed May 18 by Drs. Joseph Lawrence on "Legislation Affecting the Medical Profession"; George I. Swetlow, "Highlights in the Historical Development of Medical Jurisprudence," and Maxwell M. Boxbaum, Mount Vernon, N. Y., "The Doctor in the Witness Chair."——Dr. Harry J. Epstein, among others, addressed the Bronx Gynecological of Obstetrical Society May 23 on "Management of Delivery in Multiple Pregnancies."—— At a meeting of the Medical Society of the County of New York May 23, the speakers were Drs. James Alexander Miller on "Some Unsolved Problems in Tuberculosis" and Howard W. Haggard, New Haven, Conn., "Medical Science and Medical Progress."

Joint Group Cooperates in School Health.—A committee has been established, representing the department of health and the board of education, to coordinate problems relating to the welfare of pupils, according to the New York *Times*. The new setup will prevent duplication, loss of time and frequent overlapping of effort, it was stated. The department of health has jurisdiction over the physicians and nurses, while the board of education's bureau of health education supervises the general health program. This is the first permanent committee to be set up to coordinate action on health problems by the two departments. At a meeting to be held early this month, the scope of the committee's duties will be outlined. Under existing regulations, courses in health education are given and better health habits among the pupils are developed. It will be possible now to conduct such major projects as chest x-ray examinations for tuberculosis and other health undertakings with the cooperation of the health department. The schools will continue teaching the health habits and the health department will provide medical examinations to pupils and give "advice and counsel" to school officers.

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NORTH CAROLINA

Hospital News.—The Granville Hospital with a capacity of forty-five beds was opened recently at Oxford; it replaces the old Brantwood Hospital.——A medical library is being established at Grace Hospital, Banners Elk, in memory of the late Dr. Ronda H. Hardin, a member of the staff for many years.

University News.—Recent speakers at Duke University include Dr. Harold W. Brown, Chapel Hill, on hookworm and Vilhjalmur Stefansson, arctic explorer, on diet in primitive people. Dr. Hugh H. Trout, Roanoke, Va., conducted a clinic and showed a motion picture on radical mastoidectomy.

Seminar on Tuberculosis.—The second annual seminar on tuberculosis will be held at Asheville July 11-16. Special attention will be paid to early diagnosis and to both surgical and medical treatment. Registration will be limited to twenty and applications will be acted on in the order in which they are received; the fee is $10. Dr. Karl Schaffle, Arcade Building, Asheville, is chairman of the seminar.

Members of State Medical Board.—At the annual meeting of the North Carolina State Medical Society in Pinehurst May 4, the following members of the North Carolina Board of Medical Examiners were elected: Drs. Lewis W. Elias, Asheville; William D. James, Hamlet; Karl Busbee Pace, Greenville; Frank Alexander Sharpe, Greensboro; William M. Coppridge, Durham; James S. Brewer, Roseboro, and Lester Avant Crowell Jr., Lincolnton.

OHIO

Physicians' Orchestra.—The Doctors Symphony Orchestra gave its seventy-first concert at the City Hospital of Akron May 5. Dr. Alexander S. McCormick was director and D. H. Henninger, D.D.S., concertmaster.

Society News.—Dr. Thomas E. Jones, Cleveland, addressed the Clark County Medical Society, Springfield, recently on "Diagnosis and Treatment of the Commoner Diseases of the Colon and Rectum."——Dr. Clifford G. Foor, Hillsboro, addressed the Clinton County Medical Society recently on "Diseases of the Thyroid Gland and Their Treatment."——Dr. John E. Hoberg, Columbus, addressed the Hempstead Academy of Medicine, Portsmouth, recently on "Pyelitis in Children and in Pregnancy."——Dr. Harry L. Rockwood, superintendent of Mount Sinai Hospital, Cleveland, was elected president of the Ohio Hospital Association at its annual meeting in Columbus recently. Dr. Fred G. Carter, superintendent of Christ Hospital, Cincinnati, was installed as president.

History of Medicine in Ohio.—The Ohio Committee on Medical History and Archives of the Ohio State Archaeological and Historical Society held its first meeting at the Neil House, Columbus, May 12. The committee was organized to compile a medical history of the state. Books, reprints, transactions, instruments, prescriptions, account books, saddle bags, instrument cases, diplomas, letters, diaries, genealogies and photographs and anything pertaining to the early practice of medicine in Ohio from 1788 to 1890 are especially desired. The Ohio State Archaeological and Historical Museum will become the custodians of all the material acquired. The project is the outgrowth of a suggestion to Dr. Jonathan Forman, Columbus, editor of the state medical journal, by Robert G. Paterson, Ph.D., executive secretary of the Ohio Public Health Association, proposing the establishment of a committee on medical history. Provision was made for extension of the committee and invitations were sent to interested persons throughout the state.

OKLAHOMA

Memorial to Dr. Garabedian.—The library of the late Dr. Garabed A. Z. Garabedian was recently presented to the Tulsa County Medical Society by Mrs. Garabedian. The collection on pediatrics will serve as a memorial to Dr. Garabedian.

Society News.—The Kay County Medical Society was addressed at Blackwell recently by Drs. Arthur E. Bence and Howard C. Clark, Wichita, on "Fractures of the Spine" and "Endometriosis" respectively.——Dr. Fred E. Angle, Kansas City, Kan., discussed undulant fever before the Garfield County Medical Society in Enid May 26.

University News.—A new building for biological sciences was recently dedicated at the University of Oklahoma. The unit was financed by a PWA grant of $204,000 while $47,000 was given by the state legislature for equipment. Lorande Loss Woodruff, Ph.D., protozoologist, Yale University, was the guest speaker; his subjects were "Paramecium, Past and Present" and "Philosophers in Little Things." The dedicatory address was given by President William Bennett Bizzell, LL.D., who spoke on "The University, Biology and the State."

PENNSYLVANIA

Society News.—The Cambria County Medical Society was addressed in Johnstown June 9, among others, by Dr. William J. Mallory, Washington, D. C., on "Diagnosis and Management of the Common Diseases and Disturbances of the Digestive Tract."——Dr. George R. Harris, Pittsburgh, addressed the Armstrong County Medical Society in Kittanning June 8 on "Our Responsibilities as Molders of Public Opinion."——At a meeting of the Washington County Medical Society in Washington May 11, Drs. Guy M. Nelson and Adolph A. Walkling, Philadelphia, discussed management of gallbladder disease.

Philadelphia

Dr. Mohler Named Dean of Jefferson.—Dr. Henry K. Mohler, medical director of the Jefferson Medical College Hospital, Philadelphia, has been appointed dean of Jefferson Medical School, succeeding the late Dr. Ross V. Patterson, effective August 1. Dr. Mohler graduated at the Philadelphia College of Pharmacy. He received his degree in medicine at Jefferson in 1912, becoming medical director of the hospital in 1914. During 1913-1914 he was in charge of the laboratory of clinical medicine at the college, serving as instructor in medicine from 1913 to 1922, when he became demonstrator. He was associate in medicine from 1925 to 1929. Subsequently he served as assistant professor in medicine, associate professor in medicine and clinical professor of therapeutics.

Society News.—Among others, Drs. Maurice Muschat addressed the Philadelphia Urological Society May 23 on "Hormonal Activity in Prostatic Hypertrophy" and James F. McCahey, "The Embryological and Histological Basis for Virilism and Hermaphroditism."——The speakers before the Philadelphia Neurological Society May 27 included Dr. Gabriel A. Schwarz on "Compression of the Spinal Cord in Osteitis Deformans of the Vertebrae."——A symposium on syphilis was presented at a meeting of the Philadelphia County Medical Society May 11 with Surg. Gen. Thomas Parran of the U. S. Public Health Service as the guest speaker. Philadelphia speakers were Drs. Frederick S. Baldi, Philip Q. Roche, Baldwin L. Keyes and Daniel J. McCarthy.——Dr. Lester W. Sontag, Yellow Springs, Ohio, addressed the Philadelphia Roentgen Ray Society May 5 on "Evidences of Disturbed Prenatal and Neonatal Growth in Bones of Infants at One Month"; Drs. Jeremiah Fletcher Lutz and Lewis C. Pusch, York, Pa., spoke on "Angio-Endothelioma of Bone."——Dr. Henry P. Brown Jr. delivered the annual oration of the Philadelphia Academy of Surgery May 16 on "Acute Osteomyelitis."

Pittsburgh

Pitt Medical Alumni Homecoming.—Alumni of the University of Pittsburgh School of Medicine held its annual homecoming June 2. The program included a symposium on recent developments in therapeutics with Drs. Murray B. Ferderber, John W. Shirer, William W. G. Maclachlan and Samuel R. Haythorn and Donald A. Wilson, Ph.D., as the speakers. A smoker was also given.

The Smoke Nuisance.—A study of the smoke problem in Pittsburgh was begun early in May under the auspices of the WPA and medical and scientific societies. The program includes the measurement of smoke coming from the chimneys and smokestacks and the tabulation of information given in questionnaires. Employers and employees in the milk business have joined to effect the delivery of the health questionnaires and the newspapers and health authorities cooperated in appealing to heads of households to answer the blanks, leaving them in their empty milk bottles to be picked up by the milk drivers. In ascertaining the number of colds, sore throats and other disorders of the nose, throat and lungs reported by families, it is hoped to determine whether, in a measure, these ailments might be caused by breathing smoke into the lungs. Agencies cooperating in the study include the Allegheny County Medical Society, General Health Council, the Air Hygiene Foundation of the Mellon Institute, department of industrial hygiene, University of Pittsburgh, Singer Memorial Research Laboratory and the U. S. Bureau of Mines. Similar surveys have been conducted in St. Louis, Indianapolis and New York, it is reported.

SOUTH CAROLINA

Superintendent of Training School Honored.—A portrait of Dr. Benjamin O. Whitten, superintendent, state training school at Clinton, was unveiled April 25. The portrait is the gift of more than 100 employees at the institution. Dr. Whitten has been superintendent since the school was opened in 1920. Dr. Frederick L. Webb, medical director, presided, and F. D. Jones, D.D., director of religious activities at the school, spoke in behalf of the employees. Dr. Whitten is 51 years of age and a graduate of Atlanta College of Physicians and Surgeons, class of 1913.

District Meetings.—At a meeting of the First District Medical Society in Walterboro recently the speakers included Drs. Robert B. Taft, Charleston, "Purpura Haemorrhagica with Reference to Radium Treatment"; John W. Regan, "Use of Sulfanilamide"; Robert Wilson Jr., "Protamine Insulin"; George R. Dawson, "Blood Transfusion Technic (Review of 1,000 Cases)," and John M. van de Erve, "Color Photography for Medical and Surgical Case Records"; all are of Charleston. ——The Fifth District Medical Society was addressed in Lancaster, among others, May 11, by Drs. Carl A. West, Camden, on appendicitis; John M. Settle, Great Falls, tularemia; William B. Ward, Rock Hill, cyclopropane.

VIRGINIA

Health Department Activities.—A new full time health department will begin functioning in Buchanan County July 1. Since April 1, 1936, the county's health activities were conducted as a part of a district composed of Tazewell, Russell and Buchanan counties. Headquarters for the new unit will be in Grundy.

Personal.—Dr. William Y. Garrett, Raven, has been appointed health officer of Prince William County.——Dr. Ralph G. Beachley, deputy director of rural health in the state department of health, has been appointed health officer of Arlington County, to succeed Dr. Earle G. Brown, who recently became health officer of Nassau County, New York.

Portrait of Dr. J. S. D. Cullen.—A portrait of the late Dr. J. S. Dorsey Cullen, formerly member of the Medical College of Virginia and dean from 1886 to 1898, has been presented to the school by his grandson, Lieut. Dorsey H. Cullen of the U. S. Army. The work of Gaetan de Navaceiles, Paris, the portrait shows Dr. Cullen as a medical officer of the Confederate Army and will be placed on the walls of the library. Dr. Cullen was the son of Dr. John Cullen, one of the founders of the medical college. He was the first professor of diseases of women and children at the school, serving in this position from 1868 to 1881, when he succeeded Dr. Hunter McGuire as professor of surgery. He was a charter member of the Medical Society of Virginia and was at one time president of the Richmond Academy of Medicine.

WASHINGTON

Society News.—The King County Medical Society was addressed June 6 by Drs. James M. Bowers and Samuel T. Mercer on "Gout" and "Cutaneous Manifestations in the Leukemias" respectively. Dr. William Dressler, Vienna, discussed "Errors in the Diagnosis and Treatment of Heart Disease" at a meeting May 31. The society and its woman's auxiliary cooperated in conducting a hobby show May 23; a showing for the public was held May 24.

WISCONSIN

County Societies Sponsor Orthopedic Clinics.—Various county medical societies in the state have cooperated with the crippled children's division of the state department of public instruction in holding orthopedic clinics. Included among them are:

Outagamie County Medical Society in Appleton April 2.
Kenosha County Medical Society in Kenosha April 27.
Douglas County Medical Society in Superior May 14.
Portage County Medical Society in Stevens Point May 21.

District Meetings.—The Sixth Councilor District Medical Society was addressed at its annual meeting in Green Bay May 24 among others by Drs. Donne F. Gosin on "Segmental Enteritis"; William E. Grove, Milwaukee, "Deep Infections of the Neck" and Robert L. Cowles, "Congenital Pyloric Stenosis."——At the ninth annual meeting of the Ninth Councilor District Medical Society in Stevens Point May 5, Dr. M. Herbert Barker, Chicago, conducted a clinic on cardiovascular diseases and hypertension; he also presented a review of recent methods in the treatment of hypertension at the dinner in the evening; Dr. James M. Hayes, Minneapolis, discussed "Acute Surgical Conditions of the Abdomen" and Dr. Albert E. Rector, Appleton, president elect, state medical society, spoke.

GENERAL

Medical Journals Merge.—The *Review of Tumor Therapy* and the *Southern Surgeon* have been merged. In announcing this, THE JOURNAL, June 4, reported that financial difficulties were responsible for the change. The editors of the *Southern Surgeon* wish to correct any misapprehension concerning this journal's financial status, stating that it has "always been in the black and was never more securely so than at this time." The *Review of Tumor Therapy* was taken over by the *Southern Surgeon* and is now run as a section in the latter publication under the title of Review of Neoplasms.

Medical Section of Association for Advancement of Science.—The one hundred and second annual meeting of the American Association for the Advancement of Science will be held at Ottawa June 27-July 2. The section on medical sciences (N) will meet Tuesday and Wednesday. There will be a symposium on "Bacillus Calmette-Guérin." Wednesday the session will be a joint symposium with the Section on Chemistry (C). The subjects will include: Hormones and Immunity; Bioelectric and Other Physiological Responses of Insulin and Nutrazol; The Prolongation of the Action of Insulin; The Purification of Heparin; The Ketogenic and Anti-Insulin Properties of Anterior Lobe Extracts, and Studies on the Specific Metabolic Stimulant of Pituitary Extracts.

Winners in Syphilis and Tuberculosis Control Contest.—Tacoma, Wash., won the first award in the initial syphilis control contest sponsored this year as a part of the city health conservation contest by the United States Chamber of Commerce and the American Public Health Association. Awards of merit went to Hartford, Conn., Newark, N. J., Louisville, Ky., and New Haven, Conn. In the tuberculosis control contest, the winner is Detroit, with awards of merit going to Newton, Mass., Hartford and New Haven, Conn. Points considered by the committee were the comprehensiveness of case finding and follow-up services in connection with tuberculosis and syphilis, the facilities provided for diagnostic and treatment purposes, and the extent of group participation in programs of education and control.

Bequests and Donations.—The following bequests and donations of medical interest have recently been announced:

New York Society for the Ruptured and Crippled, $50,000; New York Medical College and Flower Hospital, $25,000; New York Foundling and Babies hospitals, $10,000 each, by the will of Mrs. Sophie March Gondran. All are in New York.

Fifth Avenue Hospital, New York, $100,000 by the will of the late Adolph L. Gondran.

Mount Sinai Hospital, New York, $35,000 by the will of William Cohen, supreme court justice.

Misericordia Hospital, New York, $25,000, and St. Vincent's Hospital, $5,000 by the will of Mrs. Harriet Brady Mathieu.

Montefiore Hospital, New York, $10,000 by the will of the late Herman Lissner.

New York Ophthalmic Hospital, New York, $2,000 by the will of the late Eliza Shardlow.

Toledo Hospital, Toledo, Ohio, will receive the bulk of an estate estimated at $2,000,000 by the will of Frank Collins.

Presbyterian, St. Luke's, Mount Sinai and Post-Graduate hospitals, New York, $50,000 each, and New York Skin and Cancer Hospital $25,000 by the will of the late Henry Ware Putnam.

Jewish and Lankenau hospitals, Philadelphia, $7,000 each by the will of the late Dr. Ellwood R. Kirby.

Methodist Episcopal Hospital, Philadelphia, $5,000 to establish the William S. Vare endowment, and $5,000 to the Hospital of the Protestant Episcopal Church for an endowment in memory of her daughter, Ida May Vare, under the will of the late Mrs. Ida Vare, Philadelphia.

Fiftieth Anniversary of Physiological Society.—The American Physiological Society observed its fiftieth anniversary at a banquet at the Lord Baltimore Hotel, Baltimore, April 1. The celebration took the form of a special program during the annual session of the Federation of American Societies for Experimental Biology and the preparation of a history of the society, the first twenty-five years being prepared by Dr. William H. Howell, director emeritus and emeritus professor of physiology, Johns Hopkins University School of Hygiene and Public Health, Baltimore, and the second by Charles W. Greene, Ph.D., Columbia, Mo., for many years secretary and more recently president of the society. Guests of honor at the banquet included four of the five living original members: Dr. Howell, Russell H. Chittenden, Sc.D., emeritus professor of biologic chemistry, Yale University School of Medicine, New Haven; Joseph Jastrow, LL.D., formerly professor of psychology, University of Wisconsin, and Dr. Warren P. Lombard, emeritus professor of physiology, University of Michigan Medical School, Ann Arbor. Dr. Frederick W. Ellis, Newton, Mass., the fifth surviving original member, could not attend. Dr. William T. Porter, Dover, Mass., was made honorary

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president for the occasion and presided as toastmaster. The late Dr. John J. Abel, emeritus professor of pharmacology, Johns Hopkins University School of Medicine, was a guest and the British and Canadian physiologic societies were represented by Drs. William H. Newton, of Bucks, England, and Charles H. Best, Toronto.

FOREIGN

Croonian Lectures.—Dr. Francis R. Fraser, professor of medicine, University of London, and director, department of medicine, British Post Graduate Medical School, delivered the Croonian Lectures of the Royal College of Physicians of London May 24, 26 and 31. His subject was "Clinical Aspects of the Transmission of the Effects of Nervous Impulses by Acetylcholine."

Prize for Work on X-Rays.—A David Anderson-Berry Gold Medal and a sum of about £100 will be awarded in July by the Royal Society of Edinburgh to the person who in the opinion of the council has recently produced the best work on the nature of x-rays in their therapeutic effect on human diseases. Applications for the award are invited; they may be based on both published and unpublished work and should be accompanied by copies of the relevant papers. Additional information may be obtained from the General Secretary, Royal Society of Edinburgh, 22 George Street, Edinburgh 2, by June 1.

Society News.—The eighth session of conferences of the International Committee on Military Medicine will be held in Luxembourg July 1-4. Colonel Voncken, Office International de Documentation de Medecine Militaire, Liège, Belgium, is in charge of arrangements.——The second congress on renal insufficiency will be held at Evian, France, September 21-24. Information may be obtained from the secretariat, 138 Avenue des Champs-Elysées, Paris 8.——The tenth International Medical Congress for Psychotherapy will be held at Balliol College, Oxford, July 29-August 2. Additional information may be obtained from the honorary secretary, Dr. Eric B. Strauss, 81 Harley Street, London, W. I.

Government Services

Cancer Center at Baltimore Marine Hospital

A new 100 bed center for the treatment of cancer patients will begin functioning in September at the U. S. Marine Hospital, Baltimore, under the auspices of the National Cancer Institute. Cancer patients of the twenty-two marine hospitals throughout the country will be eligible for the service, which will be financed by the cancer institute as one of its regular authorized activities. The new model center will give the U. S. Public Health Service facilities for cancer therapy which are too costly to maintain in individual hospitals for the relatively few cancer patients reporting to a single institution for hospitalization, and it will enable the National Cancer Institute to carry out one of the primary functions outlined in the National Cancer Act of 1937—study leading to improvement in the diagnosis and treatment of cancer. The Baltimore hospital has a capacity of 450 beds with adjacent quarters for officers and nurses, a research laboratory in addition to the laboratory for routine clinical examinations, facilities for x-ray diagnosis, physical therapy, dental and eye, ear, nose and throat clinics. Proximity to the future home of the National Cancer Institute in Bethesda, Md., was another factor in the selection of the Baltimore hospital. It is about 30 miles from the Bethesda site, where buildings of the National Institute of Health are already under construction. About 100 bed patients will be accepted at the clinic. The second floor of the hospital will be devoted to the care of bedpatients and to the admission of outpatients. Rooms in the basement will be equipped for x-ray and radium therapy and the pathologic work will be done in the research laboratory. Marine hospital patients amenable to ambulatory treatment may also be sent to Baltimore, but they will have to reside in the city at their own expense.

The cancer treatment center will be furnished with 500 milligrams of radium element and a 200 kilowatt x-ray machine, later to be supplemented with a 1,000,000 or more high voltage machine. The rooms of the hospital which will be assigned for the handling of x-rays and radium will be altered and equipped for adequate protection by the use of lead-impregnated walls and glass. It is estimated that the purchase of the radium and x-ray equipment, together with the necessary structural alterations, will cost approximately $30,000.

Foreign Letters

LONDON

(From Our Regular Correspondent)

May 28, 1938.

Nonmalignant Stenosis of the Esophagus

In his presidential address to the Section of Surgery of the Royal Society of Medicine, Prof. Grey Turner said that he had been taught that cancer of the esophagus was almost the only cause of obstruction, but he remembered a casual remark made by W. J. Mayo in 1906 that it was always worth doing a gastrostomy because the diagnosis might be wrong. During the last few years Turner had seen many examples of simple stenosis.

CAUSATION

The causation of fibrous stricture was usually obvious, generally the swallowing of corrosive fluid, but there were other causes, such as local or general infections. Milder destructive changes in the esophagus might be induced by regurgitation of very acid or toxic gastric contents and might occasionally lead to stenosis. Brown Kelly, of Glasgow, had shown that a secondary fibrosing condition might begin in association with some congenital defect.

PREVENTION

In the presence of conditions which invariably led to stenosis prevention was important. Salzer advised the passage of instruments in the early days, but this was dangerous; it was better to defer this treatment until four or six weeks after the accident. Turner had seen perforation of the esophagus by a bougie on the twenty-sixth day after the carbolic acid was swallowed. As to the ultimate condition, many patients could be permanently cured by persistent dilation, but in a few the tendency to recurrence persisted for many years and perhaps throughout life. Other methods were available. The swallowed string, usually associated with the name of Plummer, had a great field of usefulness. Turner had no success with the retrograde passage of a bougie through an artificial gastric fistula, but others had. He condemned attempts at excision of a simple stricture with end to end anastomosis. In cases which defeated the various methods mentioned there was always the possibility of making a new esophagus, but every attempt should be made to restore nature's path before trying to replace it by a surgical exploit.

Osteopath to Be Tried for Manslaughter

Though not recognized by the state, osteopathy is not only tolerated in this country but, like other forms of irregular practice, is patronized by persons of high social position and is often a lucrative business. However, meddling with a dangerous disease may prove serious, as the following case shows. A young school teacher had been under medical treatment for diabetes for some years. According to her physician her condition was satisfactory and likely to remain so provided she followed the dietetic instructions and continued with injections of insulin. She met an osteopath who told her that she had not diabetes and was suffering from anemia. His examination merely consisted of looking at her eyes and feeling her pulse. He told her to fast for four days and take orange juice every two hours. She did so and discontinued her injections of insulin. She became ill, and then the osteopath advised that she be given a little insulin in milk, but she lapsed into coma and died. The osteopath was committed for trial on the charge of manslaughter.

A Standard for Prematurity

In the compilation of the report of Queen Charlotte's Maternity Hospital, the definition of prematurity came in question. It was decided to refer it to the British Paediatric Association and the Section of Diseases of Childhood of the Royal Society of Medicine. These bodies in turn referred it to a committee

of pediatricians, who suggested a standard of 5½ pounds (2,500 Gm.) weight or under. This was circulated to various bodies, including the Royal College of Physicians and the British College of Obstetricians and Gynecologists. Neither of these was satisfied, and a further committee was set up, which included the president of the latter college, Sir Ewen Maclean, and other authorities. This committee came to the conclusion that it was impossible to define prematurity satisfactorily but that some standard was desirable for the purposes for which the proposed definition was intended. They adopted the following resolution: "That in conformity with the standard in international use an infant whose birth weight is 5½ pounds (2,500 Gm.) or less shall be considered, for the purpose of comparison of records, as either immature or prematurely born, according as the estimated period of gestation is full time or less."

Professor Boycott Is Dead

Prof. A. E. Boycott, who was a well known pathologist, has died in his sixty-second year. He was editor of the *Journal of Pathology and Bacteriology*. He became lecturer on pathology at Guy's Hospital in 1907; he was transferred to the chair of pathology at Manchester in 1912 and to that of University College, London, in 1915. At a comparatively early age he established a reputation for his studies in experimental pathology in collaboration with the late Prof. J. S. Haldane. They investigated the anemia of Cornish miners, which was supposed to be due to defective ventilation but was proved by them to be due to ankylostomiasis. Boycott's work on the blood changes in that disease and the problems connected with the passage of the larvae through the intact skin was of the first importance. In collaboration with Haldane he investigated compressed air illness (caisson disease) and showed how divers could safely be decompressed. His early work on the blood changes in ankylostomiasis led to an interest in experimental anemia and blood regeneration, on which he became a leading authority. He also was a naturalist, and snails, which he bred, were a special hobby.

PARIS

(From Our Regular Correspondent)

May 21, 1938.

Surplus of the Social Insurance Funds

An editorial in the May 14 issue of the *Journal des Practiciens* on the fate of the surplus funds collected by the social insurance authorities is of interest. The receipts from joint payments by the insured and the employers since 1930, when the law was instituted, to the end of 1936 have been about twenty-one billion francs (nearly $600,000,000). The disbursements in the form of sickness, maternity and death claims have been only about seven billion francs. All the insurance premiums paid by workers and employers do not remain in the funds of the caisses or bureaus of the social insurance organization. A certain proportion are set aside as a reserve fund; hence the caisses have received only a little over ten billion francs, so that the surplus above payment of claims amounts to three and a half billion francs up to the end of 1936. The question arises, what has become of this surplus? Large sums have been lost, according to the editorial, in lending money to politicians to be used in erection of low-priced dwellings. There has been such a lack of judgment on the part of the social insurance authorities in their investments in the form of buildings, etc., that the French treasury heads have been obliged to intervene.

Pneumococcic Encephalitis

At the May 3 meeting of the Académie de Médecine of Paris, three cases of encephalitis due to the pneumococcus were reported by Professor Marinesco and his co-workers. Three cases of pneumonia complicated by cerebral localization of the pneumococcus were observed clinically, and the condition was confirmed by studies of the brain tissue obtained at necropsy. Pneumococcic encephalitis differs from other forms of this disease. The lesions involve chiefly the white substance of the cerebrum, giving rise to areas of demyelinization with characteristics peculiar to this type of infection. In addition to the myelin tissue, the neuroglia shows evidence of intense changes of toxic origin, reacting by marked mitoses. Perivascular round celled infiltration is a third typical observation, accompanied by punctate hemorrhages in the adjacent brain tissue and blood vessels filled with fibrin. The presence of the pneumococcus in the cerebral tissue was confirmed by staining and culture.

Excessive Speed the Primary Cause of Automobile Accidents

An international bureau in Geneva forming a part of the League of Nations is analyzing statistics on the causes of automobile accidents. The first series of French statistics has recently been published by the Minister of Public Works and includes accidents throughout France during January of the present year. Although January is not a holiday month, with a large number of private automobiles on the road, there were 319 deaths and 4,164 injured in 3,471 accidents. Of these accidents, 1,371, or nearly 40 per cent, took place in Paris or its suburbs. The largest number occurred during the week end. There were 665 accidents, with fifty-one deaths, on the five Sundays and 586, with sixty-two deaths, on the Mondays; Monday is now a holiday for many people here, as a result of the forty hour a week law. The hurry of automobilists to reach their destination and to return before Tuesday, as well as the lack of knowledge of the roads by some motorists, explains the frequency of these week end accidents. The majority of accidents occurred between 4 and 8 o'clock in the afternoon, the smallest number between 3 and 4 o'clock in the morning. Collisions between motor vehicles and cyclists provide the largest number of fatal accidents. Of 2,275 collisions between motor vehicles of all types and cyclists, 516, with thirty-six deaths, were between passenger automobiles and cyclists and 142, with twenty-deaths, between trucks and cycles. Pedestrians head the list of victims of automobile accidents, with 1,367 injured and 126 killed. The occupants of automobiles, excepting drivers, come next, with 1,055 injured and fifty-two killed. The better the visibility and the better the roads, the greater is the number of accidents, indicating that speeding is responsible. Of the total of 3,471 accidents, 2,246 occurred on straight roads, resulting in 200 deaths. There were 379 accidents, with forty-five deaths, at curves and 585, with twenty-two deaths, where roads crossed.

The Incubation Period of Mumps

Drs. de Lavergne, Kissel and Accoyer, in a paper read at the May 17 meeting of the Académie de Médecine of Paris, reported having found the cerebrospinal fluid of patients in the incubation period of mumps virulent for rabbits. The fluid obtained by lumbar puncture from human beings shows a slight but distinct hypercytosis, from 3.5 to 12 lymphocytes per cubic millimeter. This meningeal reaction could only be found fifteen days after exposure to infection, thus appearing before the onset of the parotitis. The meningeal reaction remains unchanged during the period in which there are already clinical evidences of the infection. In some cases the meningeal reaction remains latent, while in others it gives rise to meningitis either before or after the appearance of the parotitis. The virulence of the cerebrospinal fluid toward rabbits and the hypercytosis of the spinal fluid have almost always been found in human beings exposed to infection who did not present signs of parotitis. This means that these persons exhibit only a meningeal localization and not a parotid one. This explains why, clinically, cases have been observed in which the infection appears only a primary meningitis. In rabbits which have been given injections of the virus into the spinal canal, meningo-

encephalitis not followed by parotitis is always observed. The conclusion reached by the authors is that the occurrence of parotitis is the most typical clinical evidence of an infection by the virus of mumps but not the most reliable or constant sign of such an infection.

Course in Bronchoesophagoscopy by Dr. Chevalier Jackson

Dr. Jean M. Le Mée, in charge of the Otolaryngological Service of the Children's Hospital of Paris, has arranged a course in bronchoesophagoscopy to be given by Dr. Chevalier Jackson, of Philadelphia, and some of his former American and European assistants. The course will begin August 23 and continue until September 1. Lectures and clinical demonstrations will be given in the Blumenthal pavilion of the Children's Hospital and operations on the cadaver at the medical school. Information in regard to the course can be obtained by writing to Dr. Jean Zhâ, assistant in otorhinolaryngology, Hôpital Necker et Enfants-Malades, 149 rue de Sèvres, Paris 15e.

BERLIN

(From Our Regular Correspondent)

May 3, 1938.

Increased Incidence of Rickets

In view of the progress made in recent years in research on vitamin D, it is surprising that an increased incidence of rickets has been reported in Germany and in other countries. This was recently pointed out by the ordinarius for pediatrics in Kiel, Prof. E. Rominger. According to several reports, the incidence of rickets among the nurslings of the Westphalian industrial region is between 37 and 46 per cent, and in the city of Dortmund it reaches 55 per cent. From Vienna an incidence of 40 per cent is reported. In the maternal consultation centers in Paris, 40 per cent of nurslings were rachitic. In Basel, Switzerland, the incidence was found to be 75 per cent during the winter and 50 per cent during the summer. Rominger himself gives for Kiel, that is, for a population of Northern Germany, as a conservative estimate 60 per cent for the winter and 40 per cent for the summer; this applies to nurslings who are brought to the clinic for consultation. Of about 1,000 school children in Munich, only 3.5 per cent were found to be free from rickets. Even more surprising are the reports about the increased incidence of rickets in high mountains, in Finland (more especially in fishing districts, in which the population practically lives on fish oil), as well as in the tropics, with the longest and most intensive exposure to sunlight that is possible. Moreover, even in breast-fed nurslings, rickets has been found more frequently in recent years, in Germany occasionally and also in Yugoslavia and in Egypt. A Norwegian investigator even found a high percentage of rachitic infants among those who had nursed at the breast for eight or nine months, and observers on the west coast of Sumatra state that rickets is frequent in spite of the fact that all infants are nursed at the breast.

Rominger believes that he has found the cause for these surprising observations: In the tropics, in Sumatra, the infants are nursed at the breast for a sufficient length of time, but the diet of the mothers is entirely inadequate. To be sure, the intensive sunlight compensates for many defects if the children are really sufficiently exposed to the sun; this, however, is not always the case, because the natives live in pile dwellings, and the young nurslings often remain confined in the house for long periods. In Germany the nutrition of the mothers is generally adequate, but nursing at the breast is not continued for a sufficient length of time; moreover, sufficient natural sunlight is not everywhere available. The conclusion is drawn that every bottle-fed infant requires prophylactic treatment against rickets. The high incidence of rickets in our latitudes can be traced to the fact that the breast feeding of infants is still not continued for a sufficient length of time and that they are fed too early with a one-sided milk-gruel diet. To be sure, it is possible that only an inadequate quantity of ultraviolet light penetrates the smoke blanket over some industrial cities. Nevertheless, rickets is almost more frequent among the children in rural regions than among the children in cities. Rominger sees the cause in the fact that instructions about this matter reach the city population more readily than the rural population.

Another cause of the frequency of rickets, which is never mentioned, Rominger sees in the inadequate doses of all antirachitic remedies. Irradiation with the quartz lamp should not be done now and again but should be done methodically. The doses of vitamin D that are given to bottle-fed infants are usually either too small or are given for too short a time or not regularly. Rominger thinks that there prevails an entirely unjustified fear of excessive doses. With many cod liver oil preparations which have been modified to improve the taste it is necessary to increase the doses in accordance with the lower vitamin D content. It is not enough to prescribe vitamin D or cod liver oil according to a fast rule; the dose must be determined in each individual case, and even for the same child it may have to be temporarily doubled or tripled, for instance, in the course of an infectious disease. In the inadequate and therefore dangerous doses Rominger sees one of the most important causes of the increased incidence of rickets during recent years. The correct dosage cannot be laid down in general rules, and it cannot be left to a lay person. In the prophylactic treatment, especial attention must be given to the right time to begin vitamin D medication in reference to the age, the time of birth and the season of the year; for instance, children born during late summer should receive vitamin D earlier, longer and in larger doses than children born during the winter. Premature infants should receive an especially early and generous prophylactic treatment.

Duration of Pregnancy

The computation of the time of birth heretofore was generally done by the method of Naegele, according to which the period of gestation is computed by counting 280 days from the first day of the last menstrual period. However, the results of a number of new investigations do not quite tally with this figure. For this reason, Dr. K. J. Anselmino, director of the women's clinic of the Rhine province, in Elberfeld, has investigated this problem on a large material. Only those cases were considered in which the labor pains began spontaneously, in which there was an exact record of the first day of the last menstruation and in which the fetus was at least 48 cm. long and weighed 2,800 Gm. With these points in view, 15,000 of the last 25,000 deliveries of the aforementioned clinic qualified for the investigation. It was found that the arithmetical mean of the duration of pregnancy, computed from the first day of the last menstruation, is 282.8, or about 283 days. It is the same for male and female fetuses, but in primiparas it is slightly longer than in multiparas. For this reason it is better for practical purposes to add not seven but ten days after the three months have been subtracted as usual. The term of 282.8 days is a mean value, around which there is a considerable dispersion of individual values. If five days is added to or substracted from 282 or 283 days, only 43.9 per cent of the women had their delivery within these ten days, whereas more than 25 per cent were not even confined within twenty days, that is, ± ten days. The determination of the true length of pregnancy, computed from the day of conception, revealed a mean value of 269 days. Since the term of conception is dependent on the length of the cycle, there are in cases of abnormally long or of abnormally short cycles apparent fluctuations in the period of gestation, which must be taken into consideration if the date of birth is computed on the basis of the last menstruation. For this reason the length of the cycle should always be considered

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when the date of birth is computed. The formula "minus three months, plus ten days" corresponds to the arithmetical mean of the length of gestation in cases in which there is a twenty-eight day cycle; for the other cycles so many days have to be added to or subtracted from the computed day of delivery, as the cycle in question deviates from the twenty-eight day cycle.

Prof. Erich Hoffmann 70 Years Old

Erich Hoffmann, for many years ordinarius for dermatology and venereal diseases in Bonn, celebrated his seventieth birthday April 25. Originally a military physician, he rapidly advanced in a scientific career. After having worked in Berlin and Halle, he became in 1910 director of the dermatologic clinic of the university of Bonn, and as such he held the chair for this specialty. He first became prominent when in 1905 he, together with Schaudinn, demonstrated Spirochaeta pallida as the cause of syphilis. He determined the presence of spirochetes in the lymph nodes of patients with acquired as well as with congenital syphilis and described a method of glandular puncture for this purpose. He demonstrated that syphilis can be transmitted by vaccination with syphilitic blood or cerebrospinal fluid. He also made contributions to the development of the therapy of syphilis. Hoffmann published a large number of papers of high merit. When, five years ago, he resigned from his professorship, the activities of this unusually energetic man did not terminate. He continued his research work in the laboratory and made lecture tours; in 1937 he made a trip of several months' duration in response to an invitation from American physicians.

CAPE TOWN

(From Our Regular Correspondent)

May 5, 1938.

The Annual Medical Congress

The annual medical congress will take place this year in September, by invitation of the Portuguese government, at Lourenço Marques. The congress is held under the auspices of the Medical Association of South Africa and the association is limited to the Union of South Africa. Negotiations between the Portuguese physicians at Lourenço Marques and the association's office at Cape Town easily overcame all organizational difficulties. For purposes of the congress the Lourenco Marques practitioners were all made honorary members of the Association, and the local organizing committee, or rather its honorary secretary and honorary treasurer, Dr. Bostock and Dr. de Carvalho, arranged an interesting program. The president of the congress is Dr. Vasco Palmeirim, senior medical officer of Lourenço Marques, while the patrons are the Portuguese ministers of education and colonies and the governor of the province of Moçambique. The Portuguese government had granted a subsidy to provide for the visit to the congress of professors of the faculties of medicine in Portugal. One problem has been that of providing accommodation for visiting members. Delagoa Bay has limited hotel accommodations and at that time of year it is one of the most popular seaside resorts in South Africa. However, the Italian Steamship Line has agreed to send the luxurious *Duilio*, now running between Cape Town and Genoa, on an excursion cruise to Delagoa Bay to provide not only transportation but accommodation for intending participants in the congress. It is anticipated that the meeting will be one of the most popular that we have had. In 1941 the association will hold a joint congress with the British Medical Association, but arrangements for that meeting have not yet been made.

Dagga Smoking

The use of Indian hemp (Cannabis sativa) for narcotic purposes is widespread in South Africa, where it has been prevalent since the days when the plant was introduced from Java at the time of van Riebeeck. Even then, however, it was found that the aborigines smoked a local plant, which they called "dagga." This plant is known botanically as Leonotis leonurus, and it is popular in gardens as an ornamental shrub. Dagga smoking has gradually been replaced by hemp smoking, but the name "dagga" has been used by the police and the public for cannabis. In consequence, confusion has arisen about the effects of real dagga smoking. A report by experts from the mental hospitals has been published in which the effects of hemp smoking are considered, but nothing is said about leonotis smoking. The effects of Indian hemp are well known and there is no difference of opinion about their cumulative toxicity, but there is a difference of opinion about the toxic effects of leonotis. It is regrettable that the name "dagga," which is historically and botanically applicable to leonotis alone, should still be attached to Indian hemp. Dagga smoking is mildly sedative and probably not more harmful to the system than moderate tobacco smoking; cannabis, on the other hand, is definitely a narcotic the use of which should at all events be regulated.

New Hospital on Cecil Rhodes Estate

The new hospital erected on the Cecil Rhodes estate and known as the Groot Skuur Hospital was recently opened and, despite the difficulties of staffing it is already working satisfactorily. So far as planning and construction are concerned, it is most interesting. The architect had to cope with several serious difficulties, among these being the problem of lighting the interior of the hospital buildings and the equally difficult problem of overcoming the effects of windage while providing adequate ventilation. Where the building stands, the southeasterly wind sometimes sweeps down the mountain slopes with a terrific velocity, creating eddies that violently disturb everything with which it comes into contact. The building was originally planned on the pavilion system, which made possible a ready solution of some of these structural difficulties, but the plan was changed to the block system. It is now a seven storied-basement block, providing scheduled accommodation for more than 800 beds, but more patients can be accommodated if necessary. At present some floors are not occupied, as it has been impossible to obtain an adequate nursing staff. The equipment is on the lines of the best American and Continental hospitals. The hospital has been designed as a general hospital. In the children's department, provision has been made for glass cubicles to permit patients with infectious diseases being nursed in the same ward. A paying block is being erected, but it is not clear yet what this addition is to serve. Apart from the fact that there is some doubt about the legality of providing such a paying ward—because the will of Cecil Rhodes prohibits the erection on any part of his estate of buildings designed for profit—there is some misgiving about the desirability of joining a paying ward to a closed institution such as the Groot Skuur Hospital must be, forming as it does the medical and surgical unit of the local university. The profession is perturbed about the innovation, and it is possible that there may be modifications of the present scheme.

Deaths in the Profession

The wastage from deaths in the profession has been considerable. Dr. D. H. Wessels, the foremost gynecologist and obstetrician in South Africa, died suddenly at the age of 56. Dr. A. B. Thomson, one of the pioneers of school medical inspection in the country, died in Natal after a lingering illness; he came to South Africa to organize school medical inspection work in Natal and later went into general practice. Dr. R. B. Thomson, who died in the same week, was the first professor of anatomy at the medical school attached to the University of Cape Town but forsook, for reasons of health, his academic work and retired to a village on the Orange River, where he contented himself with a small private practice. Other deaths during the past few months have been those of Drs. J. Duminy, George Hay, G. Munnik, L. McDowell, O. Heyns and H. N. Everard, all senior practitioners well known in the profession.

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ITALY

(From Our Regular Correspondent)

May 15, 1938.

Treatment of Rheumatic Disorders

Treatment of rheumatic disorders was the theme of discussion at a recent meeting of the Accademia Medica di Roma over which Prof. Roberto Alessandri presided.

Professor Gosio reported the treatment of rheumatism with intravenous injections of aminopyrine. The intravenous route, he said, permits the action of even small doses of from 100 to 300 mg. He held that treatment with salicylates is still an indispensable therapeutic procedure. The administration of aminopyrine, however, represents a useful and powerful adjuvant, especially for subacute and visceral rheumatism or if the administration of antirheumatic substances by mouth cannot be readily effected. Professor Arcangeli has successfully treated acute rheumatic disorders with salicylate and achieved cure within a few (three or four) days. In addition, he claims that by use of salicylates endocarditis can be prevented, cured or at least palliated and also that pericarditis and myocarditis can be favorably influenced by the same means. To obtain such results, however, it is necessary to administer intravenously, orally or rectally daily doses as high as from 20 to 30 Gm., which may gradually be decreased. By this procedure he has been able also to combat successfully the severe hyperpyrexia that often follows rheumatism and which may be a symptom of endocarditis. Aminopyrine may be usefully employed in treating cerebral rheumatism.

Dr. Poddu observed that it might be interesting to apply the method proposed by Professor Gosio to rheumatic heart disease of the nonfebrile type. The therapeutic efficacy of the method might then be evaluated by successive determinations of the erythrocyte sedimentation rate as well as by the clinical course. According to Professor Pontano, sodium salicylate is of specific therapeutic value in treating acute articular rheumatism, although in his opinion it has no demonstrable effect on concomitant endocarditis. He does not advocate extremely high doses and prefers instead daily administration of from 6 to 8 Gm. on a regular schedule of 1 Gm. every four hours. A sound evaluation of the effect of aminopyrine should result from its experimental use in the treatment of acute forms of rheumatism in children, as the internal organs of children are particularly responsive. Professor Gosio summarized the discussion, which demonstrated, he said, the uncertainties that still surround the specific action of sodium salicylate.

Absence of Dorsal Fixation of Mesentery

Prof. Tommaso Lucherini, of Rome, has studied the absence of dorsal fixation in the differential diagnosis of painful abdominal syndromes. In a report submitted to the Società di Gastroenterologia, he described three cases of absence of fixation of the mesentery, in two of which the failure was complete. One of these cases was characterized by intermittent accessional spasms, referable to the pyloroduodenal region. The attacks tended to come on at meal time, and the symptoms resembled those of duodenal ulcer. The presence of ulcers was not demonstrated by roentgen examination, and symptomatic medical therapy was followed by a measure of success. In the second case the condition began with clinical symptoms of pain referable to the right iliac fossa, which, because of its dull, protracted afebrile development, was suggestive of chronic appendicitis. After roentgenoscopic study, however, such a diagnosis was ruled out. The third case, although the defect was only partial, represented an interesting example of malformation due, according to the author's observations, to a defective rotation of the ansa media; that is, the prearterial descending section (originating in the small intestine) did not rotate, whereas the postarterial descending section (originating in the cecocolon) rotated normally. Roentgen visualization revealed the duodenum free and the small intestine dextroverted, but no inversion of the long intestine and no ulcerative or inflammatory processes. The patient was periodically seized with pains in the umbilical region, which became violently diffused in the two right quadrants and were often accompanied by emesis. This occurred at intervals of about two months. The attacks would last three or four days and were relieved by administration of belladonna and alkaline substances.

The author concludes that it is impossible to establish a certain clinical diagnosis of defective fixation of the mesenterium, since the painful and dyspeptic gastroenteric disturbances which accompany the ectopia are common to many organic lesions of the digestive tract; e. g., ulcers, appendicitis and cholecystitis. Only roentgenoscopic examination permits the sure recognition of the anomaly and then only if every segment of the digestive tract is completely visualized through mediums administered orally and by rectum. Therapeutic approach, aside from symptomatic measures, can be only by surgical intervention. The concomitant complications of absence of fixation, in addition to the morphologic and topographic alteration which facilitates the production of other lesions, are due to the particularly mobile character of the intestinal loops. If painful dyspeptic disturbances are encountered, roentgenoscopic examination is indispensable in the differentiation of intestinal dystopias from disturbances related to nervous and tonic alterations and from organic disturbances of the abdominal viscera.

Systemic Disorders of the Reticuloendothelial System

Professor Dr. Bossa has observed a case of systemic endotheliosis in a man, aged 34, who presented the symptoms of a disorder of the lymphatic system. At necropsy a reaction of the hyperplastic type was evidenced by all the lymphoglandular apparatus and the endothelium of the various lymphatics. The latter appeared macroscopically to be completely infarcted, as if a state of diffuse lymphangitis had existed, related as much to the serous membrane as to the parenchyma. No neoplastic formations were detected in any organs. Microscopic examinations showed that only the endothelium of the lymph nodes and of the lymph sinuses were involved; the normal endothelial line was no longer recognizable, and the entire lumen was occupied by large histiocytes, which showed great polymorphism of the protoplasm and of the nuclei. In reporting the results of his studies to the Accademia della Scienze Mediche e Chirurgiche of Naples, the author discussed the origin of the cells which occupy the lumen of normal lymph vessels and which may be hyperplastic and proliferative, their progressive and regressive aspect, their tendency to form syncytial masses, their manifest phagocytic activity. The study of other cells of the reticuloendothelial system, Kupffer's cells, the perivascular histiocytes and so on, evidenced their perfect integrity; of all these cells, the cells of the serous layer proper also appeared unaltered. The sum of the histologic research data formed a picture of a singular morbid disorder of the endothelial cells of the lymph nodes and of the lymph sinuses. The author proposes that this should be considered as a special form of endotheliosis.

Marriages

JOHN MILTON BARRETT, Greenville, N. C., to Miss Florence Elizabeth Schwartz of Lancaster, Pa., in Baltimore, April 27.

WALDO MASON WATTLES, Farmville, Va., to Miss Lois Wright of Fredericksburg, in Welch, W. Va., April 30.

MAURICE M. ROSENBAUM, Shallotte, N. C., to Miss Kitty Matthias of Wilmington, May 2.

HUBERT RUSSEL HATHAWAY, Madison, Wis., to Miss Lucille Grear of Riverside, Ill., in April.

CHARLES TORBERT BERRY, Greenville, Miss., to Miss Berry Stevens of Senatobia, April 28.

SAMUEL PARNELL DURR to Miss Dorothy Harker, both of Rock Island, Ill., April 23.

Deaths

Royal Samuel Copeland, United States Senator from New York, died, June 17, at Washington, D. C., aged 69. Senator Copeland was born in Dexter, Mich., Nov. 7, 1868. He received the medical degree from the University of Michigan Homeopathic Medical School, Ann Arbor, in 1889 and later studied abroad. For five years, from 1890 to 1895, he practiced at Bay City, Mich., after serving one year as house surgeon to the University Hospital, Ann Arbor, and as assistant to the professor of ophthalmology and otology at his alma mater from 1889 to 1890. He was professor of ophthalmology from 1895 to 1908. In the latter year he went to New York, where he became dean and professor of ophthalmology at the New York Homeopathic Medical College and Flower Hospital, serving for ten years. Senator Copeland was commissioner of health and president of the New York City board of health from 1918 to 1923. He became United States Senator in 1923, serving until 1929, and was reelected for terms 1929-1935 and 1935-1941. He was mayor of Ann Arbor, president of the board of education and from 1900 to 1908 treasurer of the National Board of Control of the Epworth League. He was a fellow of the American College of Surgeons and a past president of the American Ophthalmological and Otological Association. Senator Copeland was co-author with A. E. Ibershoff of a textbook "Refraction," 1906, author of "The Health Book," 1924, a "Home Medical Book," 1935, and for many years of a newspaper health column. He received honorary degrees from Lawrence University, Hahnemann College, Philadelphia, Syracuse University, Oglethorpe University and Temple University.

Thomas Lathrop Stedman ✠ New York; College of Physicians and Surgeons, Medical Department of Columbia College, New York, 1877; author of "A Practical Medical Dictionary," which has been widely used in the medical profession and of which the thirteenth edition was published in 1936; editor of the "Twentieth Century Practice of Medicine," of the "Reference Handbook of the Medical Sciences" and of "The Nurse's Medical Lexicon"; edited other medical dictionaries and handbooks, and contributed to other medical publications; aged 84; died, May 26.

Alleyne Von Schrader ✠ Lieut. Colonel, U. S. Army, retired, Palos Verdes Estates, Calif.; Washington University School of Medicine, St. Louis, 1909; entered the medical corps of the army in 1911; served during the World War; retired as a major in 1920 for disability in line of duty; was promoted to lieutenant colonel in 1930 under a special act; formerly on the visiting staff of the Community Hospital, Long Beach; aged 51; died, March 25.

Harry M. Miley, Chambersburg, Pa.; Medico-Chirurgical College of Philadelphia, 1893; member of the Medical Society of the State of Pennsylvania; veteran of the Spanish-American War; past president of the Medical Society of Franklin County; for many years member of the board of health and formerly health officer; formerly on the staff of the Chambersburg Hospital; aged 73; died, March 17.

Robert B. Campbell, Mount Union, Pa.; Medico-Chirurgical College of Philadelphia, 1895; member of the Medical Society of the State of Pennsylvania; past president of the Huntingdon County Medical Society; president of the school board; aged 73; died, March 17, in the Jefferson Hospital of prostatic hypertrophy and myocarditis.

Charles Ellis Bredt ✠ Mahanoy City, Pa.; Medico-Chirurgical College of Philadelphia, 1908; formerly assistant demonstrator of anatomy at his alma mater; at one time member of the city board of health; on the staff of the Locust Mountain State Hospital, Shenandoah; aged 57; died, March 19.

A. Howard Townsend ✠ Apollo, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1900; past president of the Armstrong County Medical Society; on the staff of the Armstrong County Hospital, Kittanning; aged 63; died, March 12, in the Western Pennsylvania Hospital, Pittsburgh.

William J. Flannery, Brooklyn; Yale University School of Medicine, New Haven, Conn., 1901; member of the Medical Society of the State of New York; formerly associate visiting surgeon to St. Mary's Hospital and St. Catherine's Hospital; aged 61; died, April 19, of carcinoma of the colon.

Edwin Stanley Cooke, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1888; served during the World War; member of the Medical Society of the State of Pennsylvania; aged 73; died, March 2, in the United States Naval Hospital, of heart disease.

William Alexander Welch ✠ Callao, Mo.; Washington University School of Medicine, St. Louis, 1903; past president of the Macon County Medical Society; formerly county coroner and member of the school board; aged 65; died, March 23, of an infection of the gallbladder.

Frank Foster Sumney, Dravosburg, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1891; member of the Medical Society of the State of Pennsylvania; formerly member of the state legislature; past president of the school board; aged 71; died, March 20.

David Barnes Cooley, Pottstown, Pa.; New York Homeopathic Medical College and Hospital, 1913; member of the Medical Society of the State of Pennsylvania; served during the World War; on the staff of the Homeopathic Hospital; aged 54; died, March 22.

Milton Tighlman McCarty, Frankfort, Ind.; Central College of Physicians and Surgeons, Indianapolis, 1902; city health officer; formerly member of the state legislature; aged 64; died, April 1, of bronchopneumonia, pulmonary fibrosis and esophageal diverticulum.

Samuel Warren Miller, Hamburg, Pa.; University of Colorado School of Medicine, Denver, 1912; member of the Medical Society of the State of Pennsylvania; aged 49; served during the World War; was found dead in March of carbon monoxide poisoning.

Abraham Royden Gregory ✠ Jacksonville, Ill.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1907; at one time assistant in ophthalmology at his alma mater; aged 59; died, April 8, of cerebral hemorrhage and hypertension.

J. Harry Pickle, Millersville, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1891; member of the Medical Society of the State of Pennsylvania; aged 75; died, March 2, of cerebral hemorrhage.

Joseph Richardson Parke, Philadelphia; College of Physicians and Surgeons, Baltimore, 1889; veteran of the Spanish-American War; aged 84; died, March 8, in the Pennsylvania Hospital of injuries received in a fall.

Glendon Franklin Sheppard ✠ Philadelphia; Temple University School of Medicine, Philadelphia, 1923; aged 40; on the staff of the Temple University Hospital, where he died, March 6, of heart disease.

Charles Edmund Ward, Little River, Kan. (licensed in Kansas in 1934); member of the Kansas Medical Society; past president of the Rice County Medical Society; aged 72; died, March 30, of pneumonia.

John Harold Fears ✠ South Bend, Ind.; Ohio Medical University, Columbus, 1903; aged 61; on the staff of the Epworth Hospital, where he died, April 9, of arteriosclerosis, uremia and hypertension.

William Johnson George, Johnstown, Pa.; University of Wooster Medical Department, Cleveland, 1881; member of the Medical Society of the State of Pennsylvania; aged 81; died, March 6, of asthma.

Cooley Baldwin Van Meter ✠ Cincinnati; Miami Medical College, Cincinnati, 1887; for many years examining alienist for the county probate court; aged 76; died, March 17, of arteriosclerosis.

Daniel Frank Gray ✠ Providence, R. I.; Bellevue Hospital Medical College, New York, 1892; on the staff of St. Joseph's Hospital; aged 74; died, April 21, of coronary sclerosis and myocarditis.

Archie Wallace Leech ✠ Beaverdale, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1911; for many years postmaster; aged 59; died, March 24, of coronary thrombosis.

Franklin Pierce Herr, Ridgely, Md.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1878; aged 86; died, March 18, of chronic interstitial nephritis.

Thomas Taylor Kirk ✠ Pittsburgh; Long Island College Hospital, Brooklyn, 1886; aged 77; died, March 16, in the Western Pennsylvania Hospital, of pneumonia.

Stephen Walter Gryczka, Reading, Pa.; Jefferson Medical College of Philadelphia, 1919; aged 49; died, March 6, in St. Joseph's Hospital, of cerebral hemorrhage.

Edward Was, Oostburg, Wis.; Rush Medical College, Chicago, 1884; aged 79; died, March 3, of hypertension and coronary thrombosis.

Henry Surville Holloman, Olla, La.; Memphis (Tenn.) Hospital Medical College, 1900; aged 59; died, April 12, of cerebral thrombosis.

Bureau of Investigation

POW-O-LIN

Another Laxative with a "Kick"

Any one at all familiar with the "patent medicine" industry knows that one of the simplest nostrums to float successfully is a laxative containing enough alcohol to impress its physiologic action on the patient. "Pep 'em up and clean 'em out!" An advertising appropriation is, of course, essential, because the business is highly competitive. But with those requirements met, business can almost be assured.

"Pow-o-lin," or, to give it its full name, "Hamlin's Pow-o-lin," is a comparative newcomer to this market and is put out by the Herb Juice-Penol Company, Inc., of Danville, Va. A Danville newspaper in August 1932 reported that James T. Hamlin Jr. had purchased the Herb Juice Company from Ben J. Lifsey of Jackson, Tenn. It is a question whether this concern really makes the "patent medicine," as the original newspaper story was to the effect that the company's products were manufactured by a pharmaceutical concern in the East and would be shipped in "bulk carload lots for preparation, bottling, labeling and distribution."

The Herb Juice Company had for some years put out a nostrum of the alcohol-laxative type under the name of "Miller's Herb Juice." Incidentally, a little over a year later—November 1933—Jackson, Tenn., newspapers reported that a state charter had been granted the Herb Products Company of that city, which the papers declared was a successor to the old Herb Juice Medicine Company, and the information was added that Mr. Ben J. Lifsey was the president of the corporation. This, however, by the way.

Herb Juice, as already stated, was a "patent medicine" laxative, the trade package of which admitted the presence of 11 per cent of alcohol—presumably the only one of the eleven drugs that the National Food and Drugs Act of 1906 requires to have stated on the label. Pow-o-lin is a "patent medicine" laxative whose carton also admits the presence of 11 per cent of alcohol. Both call for dosages of four tablespoonfuls daily —that is, 2 ounces. As the alcohol content of both preparations is about one-fourth the strength of much whisky on the market, it is easily conceivable that persons not used to alcohol might experience a feeling of well-being after taking a dose of half an ounce of a product of this type.

The present Pow-o-lin seems to be advertised mainly, if not entirely, in the South. The claims on the trade package are quite characteristic of the present day "patent medicine" exploiter. Other than stating that the product is a laxative, about the only claim made is the statement:

> "For a condition in which a remedy of this kind is indicated, satisfactory results are guaranteed when taken according to directions."

This is about equivalent to saying that for those who need this sort of thing, this is the sort of thing that such people need!

In the newspaper advertising—which, of course, is not subject to the restrictions of the National Food and Drugs Act—the claims, both direct and inferential, are considerably broader. An advertisement in a Williamsburg, Va., paper details the case of Mr. A. M. Robinson, whose picture appears with his testimonial. According to Mr. Robinson, he suffered from gas pains and nervous indigestion, which he thought were due to "a temporarily clogged intestinal tract that was brought on by my constipated condition."

A Norfolk, Va., paper carried on advertisement of Pow-o-lin with the testimonial (and picture) of Mr. R. P. White. Mr. White, like Mr. Robinson, also suffered from gas pains and nervous indigestion, which, he opined, were due to "a temporarily clogged intestinal tract brought on by neglect of constipation." The similarity of some of the phraseology of these two testimonials might cause a cynical reader to wonder if they had originated in the same advertising agency.

As a number of inquiries have come in from physicians and laymen in the Southern states, asking for information on Pow-o-lin, the Bureau of Investigation obtained an unopened, original package of this "patent medicine" on the open market and submitted it to the A. M. A. Chemical Laboratory with the request that enough work be done on it to indicate the general character of the nostrum. The Laboratory now reports the following:

LABORATORY REPORT

> "One original package of Hamlin's Pow-o-lin (Herb Juice-Penol Co., Danville, Va.) was submitted to the A. M. A. Chemical Laboratory by the Bureau of Investigation. In the trade package there was an eight-ounce flint bottle containing 240 cc. (approximately 8 fluidounces) of a light brownish liquid, possessing an odor of licorice. The reaction of the mixture to litmus was neutral. The specific gravity at 25 C. was 1.133.
>
> "No information concerning the composition of Pow-o-lin appeared on either the trade package or the label except the following declaration: 'A Vegetable Preparation . . . Alcohol 11%.'
>
> "Qualitative tests indicate the presence of an extract appearing to be licorice, a laxative (emodin bearing) drug suggestive of senna, and a sugar which reduced alkaline cupric tartrate solution; traces of sulfate and chlorides were noted. Heavy metals and magnesium sulfate were not found.
>
> "It was concluded that Hamlin's Pow-o-lin is essentially a water-alcohol solution of plant extractives flavored with licorice."

In closing, it is worth noting that on Dec. 23, 1937, the Federal Trade Commission reported that the Herb Juice-Penol Company, Inc., of Danville, Va., had entered into a stipulation with the commission to the effect that Pow-o-lin would no longer be advertised as being "capable of relieving biliousness, nervousness, indigestion and countless ills due to constipation, unless these assertions are limited to temporary relief from constipation."

Correspondence

COLLAPSE THERAPY IN PULMONARY TUBERCULOSIS

To the Editor:—In an editorial comment in THE JOURNAL, May 7, it was viewed with surprise that collapse therapy in pulmonary tuberculosis has not resulted in a greater reduction of the mortality to morbidity ratio in the tuberculosis sanatoriums. It was pointed out that Drolet's recent statistical study showed that the ratio of deaths to new cases varied little throughout various communities during a twenty year period. Lest Drolet's statistics be misconstrued as demonstrating the ineffectiveness of collapse therapy, I should like to offer an explanation for this apparent indictment.

There was published in the January 1935 issue of the *American Review of Tuberculosis* a fifteen year survey of artificial pneumothorax treatment in representative American sanatoriums. The results showed that pneumothorax treatment was given in about 10 per cent of the patients. The authors referred only to cases in which there were at least three months of pneumothorax refills. Cases in which pneumothorax had to be discontinued within three months were not included and were considered as unsuccessful attempts. This means that, a priori, about 90 per cent of the patients in the sanatoriums received no suitable pneumothorax treatment and therefore their ultimate progress was in no way a reflection on this form of treatment.

It was further found that in only 38 per cent of the cases in which artificial pneumothorax was given was an effective collapse maintained (disappearance of symptoms and bacillary sputum and closure of cavities), so that the patients who received an effective collapse were indeed a small percentage of the population of the tuberculosis institutions. It is therefore little surprising that the therapeutic results obtained from about 3 per cent of the hospitalized patients did not appreciably influence the general mortality rate.

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While there were other collapse therapy measures used besides pneumothorax, the number of patients who received pneumothorax was far greater than those who had thoracoplasties. Likewise, the number of phrenic nerve operations was not large. It may be concluded that the number of patients given collapse therapy was so small in proportion to the total number of tuberculous patients in the hospitals that it could not alter the mortality statistics even over a period of many years.

Collapse therapy is not applicable to all patients with pulmonary tuberculosis, and the percentage of patients eligible for this form of treatment has therefore been small.

The failure of collapse treatment to reduce the general hospital mortality rates does not detract from the brilliant results obtained in individual instances. These isolated results make little impression on large statistical studies but make a definite impression on the observer. During the past decade many advances have been made. Indications for treatment have been broadened, ineffective pneumothoraces have been converted into effective ones by the Jacobaeus operation, and bilateral pneumothorax has been used more extensively than before. More thoracoplasties are being done throughout the tuberculosis centers with little operative mortality. Last, but not least, is the fact that patients are presenting themselves with earlier lesions more easily suitable for treatment.

The small number of cases acceptable for collapse therapy precludes any reduction of the rate on a large scale. As time goes on the number of cases successfully treated will increase and eventually it will register in the statistics.

MILTON B. ROSENBLATT, M.D., New York.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

EXAMINATIONS DURING ANTISYPHILITIC THERAPY

To the Editor:—Because of the drive for the eradication of syphilis, I should like to know how often during treatment with bismuth compounds, arsphenamine, neoarsphenamine, tryparsamide and mercury the urine should be analyzed. What are the precautions and contraindications to these drugs as far as can be detected by analysis of the urine? Can you refer me to some literature or give me your experience of the damage that has been produced to the kidneys or other organs when these drugs have been injected and not controlled by urinalysis? Are there other precautions that you advise which the general practitioner should take who is treating or will treat syphilis? How important is the weight and blood pressure? How frequently should the eyes be examined? How often should a Wassermann test or a spinal fluid examination be taken?

P. J. IMPERATO, M.D., Brooklyn.

ANSWER.—The literature covering damage to tissue from the arsphenamines, tryparsamide, bismuth compounds and mercury is an enormous one and is summarized in such textbooks as those of Moore, J. E.: The Modern Treatment of Syphilis, Springfield, Ill., C. C. Thomas, 1933, and Stokes, J. H.: Modern Clinical Syphilology, ed. 2, Philadelphia, W. B. Saunders Company, 1936.

As far as the kidneys are concerned there is no evidence that the arsphenamines or tryparsamide, when given to persons in good general physical condition, in average therapeutic doses and when grave arsenical reactions such as dermatitis and jaundice are not produced, have any appreciable effect on the blood pressure or kidney function as measured by the phenolsulfonphthalein output or blood chemistry or on the function of other vital organs.

In therapeutic doses, furthermore, neither bismuth nor mercury produces persistent renal damage. Mercury is somewhat more likely than bismuth to cause a mild toxic nephrosis.

With any of the antisyphilitic drugs—arsenicals or heavy metals—there may be transitory albuminuria and cylindruria during treatment, though instances of serious and permanent renal damage which can be definitely and directly attributed to the therapeutic use of these drugs are exceedingly rare.

Many textbooks advise the weekly examination of the urine during arsenical treatment and immediate discontinuance of treatment in the face of mild albuminuria or cylindruria. In actual practice such frequent examinations of the urine may not be necessary, nor may it be essential to abandon treatment in the presence of mild to moderate albuminuria or cylindruria without other evidence of impairment of renal function.

All antisyphilitic drugs and particularly the heavy metals should be used with caution in the face of a previously existing nephritis or nephrosis.

The question concerning other precautions which should be taken by the general practitioner who is engaged in the treatment of syphilis is so generally phrased as to be unanswerable within the limitations of space of this column. The inquirer is advised to consult modern textbooks on the subject of the treatment of syphilis, references to two of which are given.

The weight is an important guide as to drug tolerance and caution should be exercised in antisyphilitic treatment in patients who lose weight rapidly during its progress. Blood pressure is relatively unimportant. Treatment should of course be cautious in the face of severe hypertension, especially if of the malignant variety, and in hypertension due to renal disease.

Repeated examinations of the eyes is unimportant except in the case of tryparsamide.

A blood Wassermann test may be used as a treatment guide in all patients with syphilis and, in general, should be done at the beginning and end of each arsenical course. The details of interpretation of such tests will be found in modern textbooks.

The spinal fluid should be examined in all patients with syphilis; in those with early syphilis at the end of about six months of treatment; in those with late syphilis at the start of or as soon as possible after beginning treatment. If the spinal fluid is abnormal, repeat examinations during treatment are essential.

PREGNANCY IN DUPLICATE UTERINE HORNS

To the Editor:—While performing a vaginal hysterectomy, I found double uteri, complete with tubes and ovaries for each. There was evidence of a pregnancy in each. The patient is the mother of four children. Is this condition unusual or rare?

M.D., Arkansas.

ANSWER.—Partial or complete duplications of the reproductive tract are not uncommon. This is due to the fact that the fallopian tubes, uterus and most of the vagina are derived embryologically from a fusion of the müllerian ducts. The extent of the duplication, therefore, will depend on the extent of the müllerian derivatives that have not fused. A double uterus may or may not be associated with a double vagina. In all cases, however, there are only two fallopian tubes, one arising from each horn. There are rarely more than two ovaries, one on each side.

A pregnancy in each of the two separate horns at the same time is indeed an unusual occurrence. To make this possible two separate ova would have to be fertilized at the same time and each fertilized ovum would have to pass down a separate fallopian tube to the respective uterine horn. Such a condition has been reported in the literature.

ERGOTISM AND RYE BREAD

To the Editor:—I am allergic to both wheat and yeast and as a result consume large quantities of Swedish rye bread and rye crisp. Is there any danger of ergotism?

M.D., Pennsylvania.

ANSWER.—A search of the literature has revealed no reports of ergotism in man in the United States as a result of the consumption of rye bread. Several English papers deal with the subject:

Morgan, M. T.: Report on an Outbreak of Alleged Ergot Poisoning by Rye Bread in Manchester, *J. Hyg.* **29**: 51 (April) 1929.
Robertson, James, and Ashby, Hugh T.: Ergot Poisoning Among Rye Bread Consumers, *Brit. M. J.* **1**: 302 (Feb. 25) 1928.
Stockman, Ralph: The Cause of Convulsive Ergotism, *J. Hyg.* **34**: 235 (June) 1934.
Stockman, Ralph, and Johnston, J. M.: Cereal Food Poisoning and Its Relation to the Etiology of Pellagra, *J. Hyg.* **33**: 204 (April) 1933.
Dilling, Walter J., and Kelly, R. E.: Gangrene Following the Use of Ergotized Rye Bread, *Brit. M. J.* **1**: 540 (March 31) 1928.

Morgan discusses the agricultural methods employed to prevent a fungous infection of the grain. In his opinion the ergotized grain may be eliminated in the milling process by the use of proper screening and purifying machinery. We have no information about the methods used in this country. It is probable that the United States Department of Agriculture may be able to provide some information relative to this subject.

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LILLIPUTIAN HALLUCINATION

To the Editor:—A white man, aged 42, a postal clerk, has complained for the past two years of a feeling of weakness when he is at work. He becomes nervous so that he is unable to write a money order. His sense of dimensions has become distorted, especially of height, and a table 3 feet high appears flattened to about a foot. The attacks last from fifteen minutes to an hour or more. His physical examination is negative except for a slight retraction of the left ear drum. His hearing is good in both ears. The attacks suggest a condition similar to an overdose of insulin.

M.D., New Jersey.

ANSWER.—The attacks, which are incompletely described, suggest a possible aura for a focal lesion in the occipital or temporal lobe of the brain. This lesion may be neoplastic, vascular or inflammatory. A detailed neurologic examination is indicated together with complete ophthalmologic and otologic investigations to include fundoscopy, visual fields, and caloric and turning tests. If no focal localizing signs are found it may be necessary to do either a ventriculogram or encephalogram. Neurosurgery is indicated if the lesion is neoplastic or gives any suggestion of it. This type of symptom, that is, defect in dimensions or size, is known as a Lilliputian hallucination. If the lesion is inflammatory or vascular the patient should receive some sedative such as sodium bromide. The weakness, nervousness and inability to write may, on the other hand, be due to some disturbance of the cardiovascular system and not to any cerebral disease.

POSSIBLE HYPERPARATHYROIDISM IN BOY

To the Editor:—A boy, aged 12, heretofore in splendid health, has noticed during the last four months that whenever he gets warm he becomes weak and faint and once he actually lost consciousness. His appetite is poor; he has lost 15 pounds (7 Kg.) in the last three months. During this time he has had three boils on his right hand, something he has never had before. At the beginning of his illness he had some pain around the umbilicus after he ate, which continued for two or three weeks, but since he has been eating less there has been none of this pain. His bowels have moved regularly. Physical examination reveals that he is well developed and nourished, is 5 feet three-fourths inch (154 cm.) tall and weighs 101 pounds (46 Kg.; the weight had been 115 pounds, or 52 Kg.), the temperature is 99.2 F. and the blood pressure is 120 systolic and 80 diastolic. Physical examination was essentially negative except for a cardiac rate of 100 and a heart which sounded somewhat overactive. There was a blowing systolic murmur heard at the aortic area when the patient was lying down but not in an erect position. He appeared quite nervous and seemed a little hyperactive. Urinalysis showed a faint trace of albumin. Blood counts were as follows: Nov. 24, 1937, hemoglobin 94 per cent, red blood cells 5,420,000, white blood cells 7,080, polymorphonuclears 60 per cent, lymphocytes 25 per cent, mononuclears 6 per cent, eosinophils 6 per cent, basophils 3 per cent, smear negative; December 17: hemoglobin 95 per cent, red blood cells 5,710,000, white blood cells 9,480, polymorphonuclears 47 per cent, lymphocytes 37 per cent, mononuclears 3 per cent, eosinophils 11 per cent, basophils 2 per cent; December 21: red blood cells 5,130,000, white blood cells 6,800, polymorphonuclears 46 per cent, lymphocytes 44 per cent, mononuclears 3 per cent, eosinophils 7 per cent. X-ray examination of the chest showed marked hilar infiltration but no indication of active tuberculosis. The sedimentation rate was 4 mm. per hour, the basal metabolic rate plus 3 per cent, the fasting blood sugar 83 mg. per hundred cubic centimeters, and the blood calcium 14 and 13.8 mg., tests being taken at an interval of a week. Because of the eosinophil count, three stool examinations have been made by competent laboratory men, without any parasites being found. Do you think this boy might have hyperparathyroidism? The blood calcium content suggests it. There has been no pain which is usually associated with bone changes in parathyroid tumors and, although no roentgenograms have been taken of the long bones, the bony structure of the chest and shoulders appear normal. An active rheumatic infection seems to have been ruled out by the sedimentation rate and the fact that subsequent examinations show a cardiac rate ranging from 72 to 90. Can you suggest any other diagnosis?

M.D., Tennessee.

ANSWER.—Hyperparathyroidism is surely suggested by the blood calcium levels. Blood calcium levels that remain persistently above 11.5 mg. should always be considered abnormal. The principal objection to this diagnosis is in the age of the patient. The age does not preclude such a diagnosis but it speaks strongly against such a possibility. In this case the serum calcium content should be further observed. A persistently high calcium exists for some time preceding the usual symptoms of hyperparathyroidism. A blood phosphorus determination should be made. The combination of high calcium and low phosphorus is extremely suggestive. The plasma phosphatase will be elevated also if there is detectable bone change. The urinary calcium is elevated in hyperparathyroidism but may be elevated also in other disease states. Because of the seriousness of parathyroid tumor, roentgenograms of the long bones should be made. There are detectable bone changes before the typical cysts are formed. Parathyroid tumors are rarely palpable and sometimes are difficult to find at operation.

Although the sedimentation rate argues against active infection, a number of possibilities suggest themselves and cannot be lightly discarded. A Mantoux or Pirquet test should be done. This boy is still within the age limit when hilar tuberculosis is not uncommon. A subacute bacterial endocarditis is a possibility but not a likely one. An infectious mononucleosis should be excluded. The lymphocyte count is scarcely high enough to warrant this diagnosis but a careful differential count and a heterophile antigen test should settle the question. The basal metabolic estimation should be repeated. The heat intolerance, the weight loss, the nervousness and the tachycardia are suggestive of a hyperthyroidism. The search for parasites and ova should be continued.

The fainting attacks, with one actual syncope, raise the suspicion of the effort syndrome or autonomic imbalance. Again the age of the patient makes this unlikely, but such a condition would account for all the symptoms except the hypercalcemia. One may find statements which allege that the white count as given here, that is to say, a normal total count with a relative lymphocytosis, a relative leukopenia and an eosinophilia, is sufficient to warrant such a diagnosis. The diagnosis may be safely made only when the other possibilities are ruled out.

None of these conditions, however, are consistent with persistent hypercalcemia.

WRITERS' CRAMP

To the Editor:—A man, aged 35, an auditor, is facing the loss of his job because of writers' cramp. In addition to the uncontrollable cramp he is bothered with flushing of the thenar and hypothenar eminences of both hands and occasionally slight pain in his right shoulder (he is right handed and does not stammer). His general health is excellent. There is no evidence of focal infection. There is no twitching or wasting of muscles. All laboratory tests are negative. He does not drink or smoke, sleeps well and lives a happy family life. The use of common sedatives and hypnotics has not been helpful.

M.D., California.

ANSWER.—In true writers' cramp there is no difficulty in using the hands for anything except writing with pen or pencil. If there is difficulty with every kind of use of the hands, one must look for neuritis, muscular atrophy, paralysis agitans, tenosynovitis or other organic disease. A person with writers' cramp can use a typewriter without difficulty and should do so as much as possible. If a case is not far advanced, relief may be obtained by teaching the person to write in the correct manner and the use of large cork or rubber pen holders. The cramp is often brought about by gripping the pen tightly and pressing down on the paper with unnecessary force. Attention should also be paid to the light, to the position of the paper and to the height of the desk or table. If a case is far advanced, a period of rest from writing is necessary. After this, care should be taken to observe the rules about proper writing. It is, of course, desirable for victims of this trouble to learn to write with either hand.

DIAGNOSIS OF BRAIN LESION IN CONVULSIVE SEIZURES

To the Editor:—A white man, aged 45, married, a druggist, had a severe convulsion May 16, 1936. Following the convulsion he had attacks, five or more daily, in which he was paralyzed in the left half of the body for about thirty seconds, during which time he had a profound sensation of swelling on the affected side, this sensation being more pronounced in the eye, chest and arm. With the exception of an intermission of two months last summer, he has had from three to five or more attacks daily since the onset. The mental condition of the patient is apparently normal. His weight is stationary, his appetite good and he attends to his work as usual but is nervous and worried because of his condition. The attacks come on quickly after a short prodromal feeling and he has to sit down or catch on something without delay to prevent a fall. Incidentally he has been hurt several times and has had one automobile wreck because of these attacks. Have you any suggestions for diagnosis or treatment?

M.D., South Carolina.

ANSWER.—This patient apparently has an organic disease on the right side of his brain involving the postcentral gyrus and the surrounding brain tissue. The lesion may be a brain tumor, a brain abscess, a cyst involving the cortex and meninges, an inflammatory lesion, a gumma, a syphilitic brain disease or an injury to the right cortex, or the condition may be arteriosclerosis, alcoholism or other less common disorder. The patient should have a neurologic examination, because some signs pointing to a lesion in the right side of the brain will be found. If there is no choking of the disk, an encephalogram should be made to determine the size and location of the lesion by means of ventricular deformity, pineal body shifting and presence of internal and external hydrocephalus. When this is being done a complete examination of the spinal fluid should be made, including manometric measurements to include the pressure of the spinal fluid, the amount of rise of pressure as measured by a manometer from coughing, straining and pressure on each jugular vein, a cell count, globulin determination, Wassermann test and a colloidal gold test. If there is a

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choked disk present, a ventriculogram should be made. If the air studies indicate a space-occupying lesion, neurosurgical intervention is indicated for the purpose of exposure and removal of all the lesion that is possible. If the condition is not neurosurgical an anticonvulsant regimen is necessary. This is the giving of sufficient sodium bromide or phenobarbital until the patient becomes free from attacks. When that dose is determined, the patient is kept on it for at least five years. He should not drive a car, swim, climb heights or do anything that is hazardous to himself or to any one else.

OSTEO-ARTHRITIS

To the Editor:—A woman, aged 57, weighing 165 pounds (75 Kg.), past the menopause, began having intermittent attacks of pain along the medial side of the knee joints, first one knee and then the other, six years before I saw her. The attacks until nine months ago never occurred in the two knees at the same time, never lasted more than three weeks and were never severe. She has never received an injury to either knee. The pain never has kept her from work. In April 1937, while she was having sore throat (which was unaccompanied by fever and not sufficiently severe for her to go to bed) she had the same pain in the two knee joints at the same time, much more severe than ever before. She has not been free from pain for a whole day since then. The pain is worse at night and is aggravated when she presses or touches one knee against the other. Walking has little or no influence on the pain. Weather conditions do not influence the pain. When she sits in one position for more than five minutes she has a stiffness in the knee joints with pain on rising, and the pain continues for several minutes until she has walked around for a few minutes and become "limbered up." The condition is gradually getting worse. There is a tender streak along the inner side of the knee joints, running horizontally backward and forward, exactly over the line of the joint. There are no other tender areas about the knee joints, or any other abnormalities. Anteroposterior and lateral roentgenograms of both knee joints show the same condition for the two joints: osseous overgrowth of the inner corners of the knee joints. There is no narrowing of the joint spaces or other evidences of rheumatoid arthritis. No foreign bodies were seen in the picture, which was purposely slightly light for soft tissue detail. Walking does not make the pain worse, nor does standing (she is a schoolteacher). With the leg straight and the knee fixed, outward pulling of the leg causes acute pain at the inner side of both knee joints. The opposite of this, that is, with the knee fixed, and inward pulling of the leg, causes no pain.

L. A. CROWELL JR., M.D., Lincolnton, N. C.

ANSWER.—The case is probably one of osteo-arthritis (senescent) with associated periarticular fibrositis. The cartilage is undoubtedly degenerating and fibrillated but not yet eroded or destroyed sufficiently to permit loss of the joint space. It would be well to have an estimation of the erythrocyte sedimentation rate and a differential blood smear to determine the percentage of nonfilamented cells. In atrophic (rheumatoid) arthritis the sedimentation rate is generally definitely elevated above 20 mm. (one hour) and the incidence of nonfilamented cells is more than 16 per cent. In osteo-arthritis the sedimentation rate is usually normal or nearly normal and the percentage of the nonfilamented cells is often (in 55 per cent of cases) normal.

Osteo-arthritis commonly affects elderly women about the time of the menopause and produces symptoms that may be persistent and progressive or intermittent. Studies by Garvin (1927), Keefer (1933, 1934), Bauer and Bennett (1933, 1934) and others have shown that this type of arthritis affects almost 100 per cent of persons more than 45 or 50 years of age but that only a small percentage have symptoms. The cause of the disease is unknown but it is believed to be a process of age, wear and tear and not primarily the result of infection. The various direct and indirect evidences of infection which are so commonly present in atrophic arthritis are practically always absent in osteo-arthritis.

The symptoms are generally in direct proportion to the amount of trauma endured by affected joints, whether the trauma is that of occupation or obesity or that incident to recreational pursuits. Thus patients who use their joints excessively—laborers, mechanics, farmers, women who do much housework or gardening—may have symptoms, while others may have the disease and yet remain asymptomatic. Symptoms of obese persons develop particularly in weight bearing joints, knees and the lower part of the spinal column. Patients whose threshold for pain has been lowered, by the menopause or otherwise, are more troubled than others. Pain is generally mild or moderate and intermittent. It may be subacute at times. The cause of spells of subacute pain is unknown. Excess trauma usually is blamed, but some believe that a superimposed infection may be responsible, as the case under consideration suggests. Pain in a previously affected but relatively symptomless joint may be produced by an alteration in the mechanics of the joint, by the formation of loose bodies therein, or by the pinching of sensitive synovial villi. Bauer and Bennett (1936) explained the pain thus: When marginal articular tissue is proliferating, the periosteum may become elevated and cause pain; once the marginal osteoid tissue ceases to proliferate and becomes calcified, pain may also cease. The patient referred to is experiencing "articular jelling"—stiffness after rest, relieved by limbering up. This may be attributable to capsular or periarticular fibrositis, a common accompaniment of osteo-arthritis. Symptoms of periarticular fibrositis often are brought out only, or chiefly, when the articular capsule is put on the stretch. Moderate activity often does not aggravate the symptoms of hypertrophic arthritis; in some cases it apparently does not increase the symptoms but later the joints ache more at night, probably the delayed effect of the day's trauma to joints.

The prognosis is good, although Heberden's nodes may develop on the terminal phalangeal joints of the fingers and hypertrophic arthritis of the midcervical or lower lumbar parts of the spinal column may appear. Osteo-arthritis is not associated with the constitutional reactions (loss of weight, extreme fatigue, anemia), which may become profound in atrophic arthritis. Flexion deformity, ankylosis and serious disability and crippling do not occur. The condition should be considered a nuisance, not a calamity; it should be accepted philosophically as one of the prices of living, one of the minor infirmities of age. It often becomes asymptomatic eventually, and treatment will hasten this stage. The treatment of primary importance is reassurance of the patient that serious disability is not impending. Reduction of trauma by avoidance of unnecessary walking or climbing stairs, by the use of a semielastic support for the knees, the proper type of shoes to avoid knee strain and the avoidance of obesity are imperative. The daily use at home of simple physical therapy (a heat lamp, mild nontraumatizing exercises) gives considerable relief. Roentgen therapy provides analgesia in some, but not in all, cases. Vaccines, special diets, sulfur and gold salts are apparently valueless. Obvious foci of infection which can readily be removed should be removed; others should be left alone.

SKIN STAINING FROM DIPICRYLAMINE

To the Editor:—Please give me information on the treatment of skin discoloration with dipicrylamine powder. A laboratory worker was exposed to this substance five months ago.

CLIFFORD F. LEET, M.D., Horseheads, N. Y.

ANSWER.—The fact that the skin has remained stained for more than five months argues that the chemical penetrated the epidermis and reached the deeper structures of the skin. A stain that affects only the epidermis will fade gradually and disappear.

Some substances are capable of penetrating the epidermis and in effect tattooing the skin. Such materials generally have to be used over an extended period of time and rubbed into the parts. Thus, Goeckerman reported permanent darkening of the skin from metallic substances in cosmetics which became deposited in the skin after years of usage.

If the chemical which becomes anchored in the lower layers of the skin has the property of darkening on standing, its staining of the skin may be expected to deepen in time. Some aminophenols, of the class such as the offending agent under consideration, may darken on exposure to air and light and thus intensify the stain of the skin in which they are fixed after a time.

The problem of its removal is akin to that of ordinary tattooings. The use of carbon dioxide snow might be attempted on a small patch, but this method hardly lends itself for use over a large area. This subject was discussed in THE JOURNAL, June 18, page 2100.

PHOSPHATE AND URATE KIDNEY STONES

To the Editor:—A white man, aged 32, during the last six years has had three small renal calculi, visualized by x-ray examination and small enough to have been passed through the ureters and the urethra. Although he has been drinking ten or twelve glasses of water daily, the urine always shows a large deposit of crystals. The deposit appears to be about the same quantity whether the urine is acid or alkaline. Two of the calculi have been of phosphate composition and one of urate. He has been on a low purine and low mineral diet at various times without any apparent change in the amount of crystalline deposit in the urine. The condition is complicated by a chronic nonspecific prostatitis, at times acute, apparently after an upper respiratory infection, which has responded on two occasions to sulfanilamide therapy. On large doses of vitamin A there has been no change in the urine. The renal function as tested by dye excretion, concentration test and blood chemistry is normal. The blood calcium and phosphorus levels are also normal. The urine obtained by ureteral catheterization has been free from pus. Is there likely to be any relationship between the chronic prostatitis and the formation of the renal calculi? Is there any dietary regimen which might prevent the excretion of the large amounts of crystalline material?

ALEXANDER G. SILBERSTEIN, M.D., New York.

ANSWER.—In view of the fact that the calculi have been of phosphate composition and also of urate composition on one occasion, the continued use of an acid-ash diet with a low purine content would be advisable. This dietary regimen will probably reduce the amount of crystalline deposit in the urine

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more than any other. The importance of chronic prostatitis as a factor in stone formation is not definite, but in persons who are prone to form urinary calculi the eradication of all foci of infection seems definitely indicated. The teeth and tonsils should be examined carefully and any necessary corrections should be made. A regular course of prostatic massage twice weekly over a period of from eight to ten weeks seems indicated. Occasional doses of sulfanilamide should be of help. According to the work of Higgins, it would also be well to maintain an adequate vitamin A and D intake.

Many of these persons apparently have a cycle in their lives in which they form urinary calculi. This may continue for a period of years and then without any apparent change in treatment or manner of living the formation of stones will cease. Until that period arrives the suggested regimen should be followed. It has been tried in other cases with beneficial results.

VOMITING OF PREGNANCY

To the Editor:—Please give me some information on the treatment of hyperemesis gravidarum. What is the value of estrogen? What is the suggested dosage? Has the use of adrenal cortex extract proved successful enough to merit its use? LUTHER M. HIGH, M.D., Millersburg, Ohio.

ANSWER.—Before a diagnosis of hyperemesis gravidarum is made, the physician must be certain that the patient is pregnant. This may be difficult during the early weeks of gestation without the aid of an Aschheim-Zondek test. Furthermore a careful examination must be made to determine a possible extragestational cause, such as gallbladder disease, gastric or duodenal ulcer or other ailments. If the case is one of hyperemesis, the physician should use psychotherapy in conjunction with whatever medication is employed. In some cases, especially mild ones, psychotherapy alone produces spectacular success. In most severe cases, however, the patient must be strictly isolated, preferably in a hospital, and fluids and food must not be given by mouth for at least twenty-four or forty-eight hours. Dextrose and an abundant supply of liquids should be administered intravenously, and sedatives in large doses and at regular intervals should be given by rectum. When improvement occurs, solid food and liquids should be given by mouth, at first in small amounts and then in increasing quantities.

One of the most satisfactory ways to feed a patient who has hyperemesis is by means of a duodenal tube. Through the latter it is possible to give large quantities of fluids, carbohydrates, proteins, fats, minerals, vitamins, laxatives, sedatives, and so on. The tube may be left in place for many days, until the patient is built up to a point at which she will be able to take food and liquids by mouth.

Various remedies have been advocated during the last few years and all have helped some patients, if not by their physiologic activity then by their psychic effects. Iodine in the form of the compound solution is of benefit in many cases. Insulin has helped in some cases but this substance must be used with great caution and preferably in combination with dextrose. Adrenal cortex extract has been used in many cases and some reports are enthusiastic about the results (Freeman, William; Melick, J. M., and McCluskey, D. K.: *Am. J. Obst. & Gynec.* **33**:618 [April] 1937). The same enthusiasm has been expressed for the use of cevitamic acid (Dicker, Serge: *Schweiz. med. Wchnschr.* **67**:74 [Jan. 23] 1937). Likewise benefit is claimed for the use of parathyroid extract along with calcium (Sussmann, Walter: *Am. J. Obst. & Gynec.* **33**:761 [May] 1937). Some patients have been benefited by having their own urine instilled into the rectum (Fischer, *Med. Klin.* **32**:1298 [Sept 18] 1936).

Recently it was found by McGowan, Baker, Torrie and Lees (THE JOURNAL, Feb. 12, 1938, p. 498) that the vomiting of pregnancy sometimes is associated with a spasm of the second portion of the duodenum with probably a decrease in tone of the pylorus and stomach. These authors found that glyceryl trinitrate satisfactorily controls a certain number of cases of vomiting of pregnancy.

As far as is known, estrus-producing substances have no specific effect in hyperemesis gravidarum. If valuable at all, they most likely act because of their psychic effect.

A physician treating a severe case of hyperemesis must watch the patient carefully. Attention should be paid not alone to the general condition of the patient but also and especially to the pulse, temperature, blood and urine. The disease is frequently treacherous and, in spite of apparent progress, some patients die. It is better to empty the uterus too early than permit the proper time to slip by, beyond which even a therapeutic abortion will be of no avail. Of course, in every case in which interruption of the pregnancy is contemplated, a second physician should be called in consultation.

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, June 28. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ALASKA: Juneau, Sept. 6. Sec., Dr. W. W. Council, Box 561, Juneau.

ARIZONA: Phoenix, July 5-6. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: Little Rock, Nov. 3-4. Sec., State Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, Texarkana.

CALIFORNIA: *Reciprocity.* Los Angeles, July 11, San Francisco, Sept. 14, and Los Angeles, Nov. 16. *Written examinations.* San Francisco, June 27-30, Los Angeles, July 11-14, and Sacramento, Oct. 17-20. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: Denver, July 6-8. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Medical (Regular).* Hartford, July 12-13. *Endorsement.* Hartford, July 26. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Medical (Homeopathic).* Derby, July 12. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: Dover, July 12-14. *Reciprocity.* Dover, July 19. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science.* Washington, June 27-28. *Medical.* Washington, July 11-12. Asst. Sec., Commission on Licensure, Mr. Paul Foley, 203 District Bldg., Washington.

HAWAII: Honolulu, July 11-14. Sec., Dr. James A. Morgan, 48 Alexander Young Bldg., Honolulu.

IDAHO: Boise, Oct. 4-5. Commissioner of Law Enforcement, Hon. J. L. Balderston, 205 State House, Boise.

ILLINOIS: Chicago, June 28-July 1, and Oct. 18-20. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

IOWA: *Basic Science.* Des Moines, July 12. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MAINE: Augusta, July 5-6. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MASSACHUSETTS: Boston, July 12-14. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413-F State House, Boston.

MONTANA: Helena, Oct. 4. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEVADA: *Reciprocity.* Carson City, Aug. 1. *Applications must be completed and on file by July 17.* Sec., Dr. John E. Worden, Capitol Bldg., Carson City.

NEW HAMPSHIRE: Concord, Sept. 15-16. Sec., Board of Registration in Medicine, Dr. Fred E. Clow, State House, Concord.

NEW MEXICO: Santa Fe, Oct. 10-11. Sec., Dr. Le Grand Ward, 135 Palace Ave., Santa Fe.

NEW YORK: Albany, Buffalo, New York, and Syracuse, June 27-30 and Sept. 19-22. Chief, Professional Examinations Bureau, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH DAKOTA: Grand Forks, July 5-8. Sec., Dr. G. M. Williamson, 4½ S. 3rd St., Grand Forks.

OKLAHOMA: *Basic Science.* Oklahoma City, Dec. 7. Sec. of State, Hon. Frank C. Carter, State Capitol Bldg., Oklahoma City.

OREGON: *Basic Science.* Corvallis, July 16 and Portland, Nov. 19. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene.

PENNSYLVANIA: Philadelphia and Pittsburgh, July 5-9. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

PUERTO RICO: Santurce, Sept. 6-10. Sec., Dr. O. Costa Mandry, Box 3854, Santurce.

RHODE ISLAND: Providence, July 7-8. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, June 28. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA: Rapid City, July 19-20. Director of Medical Licensure, Dr. B. A. Dyar, State Board of Health, Pierre.

WASHINGTON: *Basic Science.* Seattle, July 14-15. *Medical.* Seattle, July 18-20. Dir., Department of Licenses, Mr. Harry C. Huse, Olympia.

WEST VIRGINIA: Elkins, July 4-6. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: Milwaukee, June 28-July 1. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the *National Board of Medical Examiners* and *Special Boards* were published in THE JOURNAL, June 18, page 2105.

Idaho April Examination

Hon. J. L. Balderston, commissioner of law enforcement, reports the written examination held at Boise, April 4-6, 1938. The examination covered sixteen subjects and included 160 questions. An average of 75 per cent was required to pass. Thirteen candidates were examined, all of whom passed. The following schools were represented:

School	PASSED Year Grad.	Per Cent
Stanford University School of Medicine	(1934)	86
University of California Medical School	(1936)	87
George Washington University School of Medicine	(1937)	81
Northwestern University Medical School	(1938)	80
Rush Medical College	(1937)	83
Washington University School of Medicine	(1936)	83
Creighton University School of Medicine	(1933)	83
University of Oregon Medical School	(1937)	88
University of Pennsylvania School of Medicine	(1936)	88
Vanderbilt University School of Medicine	(1937)	87
Marquette University School of Medicine	(1926)	90
University of Alberta Faculty of Medicine	(1930)	93
University of Manitoba Faculty of Medicine	(1923)	93

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Book Notices

Fifty Years a Country Doctor. By William N. Macartney, M.D. Cloth. Price $3.50. Pp. 584, with portrait. New York: E. P. Dutton & Company, Inc., 1938.

This is the story of a doctor who began life in a small town in New York on the St. Lawrence River, got his preliminary education in the schools of the town, went to medical school for two years in New York City, had an internship in Bellevue Hospital, and then went back to his home to practice in order to be with his parents in their old age. Eight years later, when they had died and he had accumulated enough to cover the lean years that he would have in establishing himself in New York City, where it was his original ambition to practice, he went back there, looked around long enough to decide that to practice in Fort Covington, among the people he knew, was his choice, went back home and has devoted the last forty years to practice there. He graduated in 1888. The town had a population of 600 then; in 1936 it had a population of 764, so this is the story of a real country doctor. It is a story also of a vigorous mind, alert, quick, independent. The book describes a fine life. He is a sympathetic man, but the book has no sob-stuff. It is full of interesting episodes with many good stories—told briefly—and vivid accounts of practical experiences in taking care of difficult emergencies, usually alone.

After a good chapter on his youth, the next chapters are devoted to his experiences at medical college and at Bellevue. It happens that the reviewer was a member of the same class in the same medical school, and he can testify to the accuracy of the descriptions of conditions. The brief sketches of the members of the faculty are by one who has more than the ordinary capacity for hitting off the characteristics of men and make one more inclined to take at their face value all of the later statements. Once in a while, however, a mistake is found, as when, apropos the blizzard in New York in 1888, he said "In those days we had no weather bureau" (p. 37).

The next seventeen chapters are short—as are all the chapters in the book—and are devoted to the general topics that concern the doctor, particularly the country doctor: beginning in practice, advances in technic, characteristics of patients, fees, the dead beat and things of that sort. They are full of worldly wisdom, in the best sense of that term, that has been matured by long experience in a busy important life. The remainder of the book is devoted to consideration of the common diseases and contains many acute observations and wise practical suggestions.

He is a cheerful soul and must have enjoyed life. His style is sprightly, he writes good clear English, and the book is entertaining reading. It is a fine exposition of the attractiveness of a country practice to a competent man. The first fifteen chapters, only 135 pages of easy reading, ought to be read by all senior medical students.

Lettres à un jeune praticien sur les maladies de l'anus et du rectum. Par Roger Savignac. Préface du Professeur A. Gosset. Paper. Price, 26 francs. Pp. 129. Paris: Masson & Cie, 1937.

The author's plan of presentation in this book is indeed unique. Presumably he has been asked by a young doctor for his advice and experience relative to the more common anorectal diseases. Savignac's background is a twenty year period of service as director of the proctologic clinic of the Salpêtrière. He makes his contributions to the "young practitioner" in the form of a series of letters, fourteen in all, each one covering a specific subject. The work serves admirably first to make the practitioner conscious of anorectal disease and then to instruct him in the performance of a thorough examination, both digital and endoscopic. The author considers his patient to have a serious ailment until such has been ruled out by thorough investigation. He has placed proper emphasis on the serious nature of chronic ulcerative colitis and of inflammatory rectal stricture. With regard to the etiology of the latter entity he feels that our present conception is still hypothetic. The author has purposely avoided discussion of surgical technic other than that pertaining to the agents of physical therapy such as medical and surgical diathermy. As a result, so much emphasis is placed on the ambulatory or office treatment of hemorrhoids, fissures and fistulas that the work smacks a bit of the "ambulant proctologist." One cannot help but fear that the young doctor will be led to place too much faith in nonsurgical methods and that he may not be brought to realize the full significance of anorectal infections. No one cares for unnecessary surgical procedures. However, most patients suffering from fissures, fistulas or complicated piles are deserving of hospitalization for proper surgical treatment. The sections on fissure and fistula are at once both pleasing and disappointing. With regard to anal fissure the author advocates three forms of treatment: electricity (diathermy), local injections and dilation under anesthesia. Anal abrasions might be amenable to such therapeutic endeavors, but true anal fissures, in the experience of well trained proctologists, yield only to proper surgical treatment fortified by thorough and persistent after-care. In his "letter" on anal fistula the author emphasizes surgery as the only adequate form of treatment. However, when mention is made of "blind" fistulas, of injections of methylene blue to facilitate visualization of the tract, and of x-ray studies after injection of colloidal thorium dioxide or of iodized oil one cannot help but feel that the author does not possess a full conception of the pathogenesis of fistula-in-ano. The final letter is a brief review of the causes of "anorectal" hemorrhage in the order of their frequency and significance. The book is a valuable addition to the literature of diseases of the anorectum and colon. It should be read by the general practitioner, by the gastrointestinal internist, by the general surgeon and by the rectal surgeon.

Physical Exercises for Asthma. Approved by the Honorary Medical Advisory Committee of the Asthma Research Council. Second edition. Paper. Price, 1s. Pp. 32, with illustrations. London: Asthma Research Council, King's College, 1937.

The brochure is written for the layman as well as for the physician. The purpose of the exercises described, as stated in the introduction, is to correct the shortening of the muscles of respiration which occurs in asthma. The contraction of these muscles produces the "barrel-shape" chest. Because of this the lungs remain distended even when the patient is free from attacks. In early cases the purpose is to prevent such occurrence. In chronic cases the attempt is to restore the chest cavity and lungs to normal size. In asthma the tendency is to breathe almost entirely with the upper part of the chest, the lower part of the chest remaining relatively immobile. The diaphragm moves little. The exercises are aimed to teach the patient "diaphragmatic breathing," to use the abdomen and lower part of the chest as well as the upper part of the chest. Three groups of exercises are described. Each is simply explained and adequately illustrated by reproductions of photographs. There are five elementary exercises, five advanced exercises and four children's exercises. While each is intended to exercise a different group of muscles, the breathing principle is the same in all—a short inspiration through the nose, followed by a gentle, prolonged expiration through the mouth. During the expiration the patient makes an F or S sound with the lips or teeth to fix his attention on blowing out as long as possible. During inspiration the upper part of the chest must remain still, the abdominal wall rising during this phase. With expiration the abdominal wall contracts slowly. It is recommended that exercises be practiced for at least ten minutes twice a day. The value of exercises as an adjunct in the treatment of asthma has been recognized for many years. As pointed out in this pamphlet, they should, however, be supervised at the start by a trained person. While these exercises can be of help, they will be sure to fail unless the physician or a trained gymnast supervises them until the patient does them correctly.

Sixteenth Hospital Yearbook. 1938 Hospital Purchasing File: Directory of Products, Manufacturers' Catalogs, Purchasing and Other Reference Data. Boards. Price, $2.50. Pp. 838, with illustrations. Chicago, Illinois: Modern Hospital Publishing Co., Inc., 1938.

This book is a standard reference on hospital buying. It contains extensive catalogues on clinical and scientific apparatus, general furnishings, food service equipment, laundry supplies and construction materials. To hospital executives it also presents a valuable section on purchasing and other reference data relative to the planning of ward and private services, surgical facilities, outpatient, maternity, pediatric and psychiatric departments, the tuberculosis unit, contagious disease wards, x-ray and physical therapy departments, laboratories,

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the nurses' home, the school of nursing, kitchens and the hospital laundry. Special articles give authoritative information on the quality and performance of hospital equipment and supplies and should be of distinct value to purchasing agents. There is a useful description of typical hospital positions, a list of state, sectional and Canadian hospital associations, current hospital statistics, per capita costs and occupancy figures. The administrative departments of hospitals will find the Yearbook a valuable source of reference. Its use is enhanced considerably by a convenient index of catalogues and advertisements, a directory of hospital products covering 217 pages, a guide to purchasing and other reference data, and useful check lists of departmental equipment and supplies.

Untersuchungen über die Augenhöhlen des Menschen in verschiedenen Lebensaltern. Von Per Pallin, Med. Lic. Inauguraldissertation welche mit gehöriger Genehmigung der welterfahrenen medizinischen Fakultät zu Uppsala verteidigt wird. Sonderabdruck aus Acta Societatis medicorum Suecanæ Bd. LXIII, 1937. Paper. Pp. 107, with 22 illustrations. Stockholm: Isaac Marcus Boktryckeri-Aktiebolag, 1937.

In this dissertation from the University of Uppsala, produced under the direction of Professor Berg, ophthalmologist, and Professor Agduhr, histologist, Pallin investigates the evolution of the orbit from fetal to adult life. Ample material at various ages has been systematically analyzed according to accepted modern biometric procedure, and the data provided should facilitate a better visualization of the mechanism of orbital development. At the beginning of the second month of embryonic life the eyes look laterally, reminiscent of our phylogenic ancestry, and the optic stalks are in line with each other. The angle is reduced to 105 degrees in the next month, reaches 71 degrees at birth, and converges from 3 to 5 degrees further by maturity. In late childhood the expansion of the facial skeleton increases the orbital and interorbital width much more than the distance between the optic foramens, occasioning consequently a forward divergence of the orbital axes and of the associated cone of ocular muscles. In this connection the author seriously considers the contention made by Weiss forty-five years ago that this developmental process accounts for the occasional spontaneous correction after puberty of low degrees of convergent squint but fails to discuss the various other anatomic and physiologic factors to be considered. In view of these changing relations of the orbit from birth to maturity, the associated changes involved in maintaining parallel vision is an interesting inquiry that should repay further study.

The Basis of Tissue Evolution and Pathogenesis. By Albert A. Gray, M.D., F.R.S.E. Cloth. Price, 7s. 6d. Pp. 92, with 12 illustrations. Glasgow: Jackson, Son & Company, 1937.

Those who are conversant with Albert A. Gray's large and comprehensive two volume work on "The Labyrinth of Animals" will little wonder that this clinician and investigator should subsequently be writing on problems pertaining to evolution. His extensive studies on the comparative anatomy of the intricate and delicate inner ear naturally led Gray to ponder over the problems of origin and variation. Then too his observations and contributions in the field of clinical otology, especially otosclerosis, afforded opportunity for reflection in the field of pathogenesis. Whether or not entirely in accord with the concept of Gray on tissue evolution and pathogenesis, one cannot but admire him for his spirit and industry in subjecting his clinical problems to scientific laboratory scrutiny.

From the beginning, Gray appears to have given thought to the manner in which the structure of plants and animals may have evolved in direct relationship to environment. He had intended to publish a book giving his matured views on this subject but died before this could be fully consummated. Fortunately he left a manuscript, and his younger son, conversant with the subject matter, assumed the responsibility for publishing posthumously his father's last work.

After the foreword, the book is divided into four parts, on the basis of tissue evolution and pathogenesis, evolution of the tissues, repair, and evolution of tissues and structures. At the outset Gray deprecates the narrow view of pathogenesis often held, aptly saying that in all pathologic processes there is present a soil and a seed. He holds to the concept that disease processes are merely one manifestation of biologic processes and that they cannot be considered apart from the ordinary problems of biology. When he speaks of an injuring agent, he has in mind the environment of the organism or tissue. The point is made that the direct observation of the behavior of a tissue toward an injuring agent and its evolutional fate must be impossible at all times, since the process itself must extend over vast periods. Gray here speculates "upon the evolution of the tissues, using as a basis the accumulated knowledge of biological and pathological processes, and particularly the process of repair in living tissue." He appreciates that "from the very nature of such problems, some amount of speculation is absolutely necessary" but says that "even then it will be possible to bring considerable evidence from observed facts in support of the views advanced."

Gray feels that the process of repair acquires a very real biologic significance, quite apart from the usual teleologic explanation so widely accepted. He suggests that the change in the character of a given tissue, the metaplasia, is the basis of the evolution of species and is a fundamental factor in pathogenesis. He would substitute the concept of "induced variation" for the doctrine of "spontaneous evolution." He makes much of injury, that is, environment, and the fact that ultimately environmental factors may lead to fixed and new conditions of tissues, with even a heritable tendency. He attempts to correlate his hypothetic concepts with his daily clinical problems.

In the foreword of the book, the wish is expressed that those who read its pages will do so with insight and imagination. The volume merits reading.

Theoretical Principles of Roentgen Therapy. Edited by Ernest A. Pohle, M.D., Ph.D., F.A.C.R., Professor of Radiology, University of Wisconsin, Madison. Foreword by W. Edward Chamberlain, B.S., M.D., F.A.C.R., Professor of Radiology in the Temple University School of Medicine, Philadelphia, Pa. Cloth. Price, $4.50. Pp. 271, with 132 illustrations. Philadelphia: Lea & Febiger, 1938.

This book is a collective work. The demand for knowledge of the physical, chemical and biologic basis of roentgenology has increased. The physics of x-rays by Stenstrom Newell provides a review of the various aspects of therapeutic x-ray equipment; he describes the instruments for calibration (tubes, filters and other materials necessary for roentgen treatment, such as tables, control stands and the proper choice of space). Taylor and Pohle consider dosimetry. Superficial and depth doses and the relation to the percentage volume are distinctly treated, and the difference in their application is described. The importance of a definite plan of treatment is well developed. In a further chapter, Ward discusses radiology and radiopathology; that is, the reaction of cells, skin, tissue, blood and internal organs to the x-rays. Finally, Taylor develops the idea of the tolerance dose and protection from the x-rays. The recommendations of the Advisory Committee on X-Ray and Radium Protection have been copied verbatim.

An Atlas of Gas Poisoning. Reprinted by the Home Office (Air Raid Precautions Department). Second edition. Paper. Price, 35 cents. Pp. 16, with 11 illustrations. New York: British Library of Information; London: His Majesty's Stationery Office, 1937.

This booklet is one of a number of excellent handbooks and pamphlets issued by the home office of the British government, presenting various phases of warfare as it may affect the civilian population and intended primarily for civilian use. From its rather broad title one would perhaps expect a more comprehensive treatment of the subject, for, with the exception of a single plate depicting a rare case of thrombotic gangrene of the foot following chlorine poisoning, the pamphlet confines itself to the effects of but two warfare agents, phosgene and mustard. Presenting these, however, as respectively representing pulmonary irritants and vesicants—the two classes of chemical warfare agents used primarily for the production of casualties among personnel—the atlas handles them well: ten colored plates, three relating to phosgene and seven to mustard, picture the principal clinical and pathologic effects of these two agents; and the accompanying descriptive text is clear and concise. The pamphlet is a second edition, the first having been published in 1918 for use by medical officers serving with the British Expeditionary Force. As stated in the foreword, the present edition reproduces substantially the same text and drawings as the first edition, with minor textual revisions in the light of later knowledge; and its primary aim is that of general instruction for doctors not already familiar with the subject. Toward this end, the atlas is an authoritative and valuable help.

Précis de chimie organique. Par Victor Grignard, membre de l'Institut (Prix Nobel). Publié par les soins de Roger Grignard, ingénieur-chimiste E.C.I.L., préparateur à la Faculté de sciences de Lyon, et Jean Colonge, ingénieur-docteur, chef de travaux à la Faculté des sciences de Lyon. Préface de M. le Professeur G. Urbain, membre de l'Institut. Cloth. Price, 175 francs. Pp. 774. Paris: Masson & Cie, 1937.

Victor Grignard, Nobel laureate, commands such respect among organic chemists that anything bearing his name must be treated with more than ordinary consideration. It is true that this book is posthumous, but it is completed as a token of respect and veneration. One would expect, therefore, and finds, unusual care and precision in the work. It is stated in the introduction that the book reproduces faithfully the course given by Victor Grignard, each year, to candidates for the certificate of general chemistry in the School of Industrial Chemistry at Lyons. It is therefore a textbook the worth of which is proved. Organic chemistry is a subject as logical as geometry. No unusual order of presentation is to be expected or found. The order is much the same as is found in standard textbooks. Following a chapter on general fundamental principles, the following plan is followed: aliphatic and cyclic hydrocarbons, organic metallic compounds, alcohols, phenols, thioalcohols and thiophenols, aldehydes, ketones, sugars, cetenes, acids, amines, albuminoids, nitrils, amides, heterogenic cyclic compounds. The treatment is strictly scientific. When such subjects as ethylene and cyclopropane are discussed, no mention is made of their uses in anesthesia. Quinine, he states, has been used a a febrifuge since the seventeenth century, the historical fact apparently, and not the practical use, being the more interesting. The book is written with a clearness to which the French language lends itself, but even as a French work the clearness of expression is notable. It is an excellent textbook and is an honor to the memory of a man who needs no added eulogy.

Report on Progress of the Works Program December 1937. Harry L. Hopkins, Administrator, Corrington Gill, Assistant Administrator, and Emerson Ross, Director, Division of Research, Statistics and Records. Paper. Pp. 112, with illustrations. Washington, D. C.: Works Progress Administration, 1938.

Nearly $9,000,000,000 had been distributed up to Oct. 31, 1937, which at the maximum gave relief in the form of work to more than 3,000,000 persons. Projects, which were approved in all cases by local authorities, include highways, public buildings, parks, conservation, airports and a wide variety of "white collar" and educational activities. Special mention is made of the Carrie Tingley Hospital for Crippled Children at Hot Springs, N. M., the Milwaukee Sewing Project, which during the six months from April through September 1937 produced more than 840,000 garments, and various public works. A sample of 1,595,000 workers in August 1937 showed that 64 per cent of them were unskilled and only 5 per cent professional and technical workers. The National Youth Administration, by the expediture of $122,233,050 in 1936 and 1937 aided 400,000 youths each year in obtaining an education. Various research projects, especially some in regard to the effects of technologic development, were conducted.

Chiropody: Theory and Practice. By Franklin Charlesworth, F.B.A.Ch., Founder of the British Association of Chiropodists. Foreword by W. Sayle Creer, M.Ch., F.R.C.S. Second edition. Cloth. Price, 15s. Pp. 205, with 57 illustrations. London: Actinic Press, Ltd., 1938.

The first part of the book is a review of the anatomic structures of interest to the chiropodist. The author warns the chiropodist that many of the conditions which the latter is called on to treat can be successfully handled only by a qualified surgeon. The writer of the foreword to the first edition calls attention to the fact that modern fashions in footwear and overindulgence or carelessness in the pursuit of various sports have increased the frequency of foot complaints. There is today a large number of persons who are attempting, with and without training or qualification, to deal with them. The manuscript has been reviewed, read and corrected by an orthopedic surgeon. Chapters on the anatomy and physiology of the foot and lower part of the leg are given in some detail in order to lay the groundwork for the second part of the book. The author discusses osteology, connective tissues, ligaments of the knee, ankle and foot, muscles of the leg and foot and arteries and veins of the leg and foot, and the nervous system. Some of the conditions mentioned are taken care of by little more than a definition, which is just about all the space they deserve in this type of book. The information appears to be accurate, much of it having been taken from other sources of anatomy and physiology. The chapter on foot orthopedics is satisfactory. The chapter on pads and domes and strappings is good. The chapter on ringworm of the foot is weak. If the author had used the space occupied by the respiratory condition for elaboration of the treatment of ringworm—which is so common and important—it would have enhanced the value of the book. The case notes from the foot hospital are commendable.

Introduction and Guide to the Study of Histology for Students in Medical Schools and Colleges. By Avery E. Lambert, Ph.D., Professor of Histology in the School of Medicine, State University of Iowa. Cloth. Price, $5. Pp. 542, with 185 illustrations. Philadelphia: P. Blakiston's Son & Co., Inc., 1938.

The descriptive matter of this book is written from the point of view of the older textbooks and is based on the data they contain. Most of the illustrations are the well known semidiagrammatic figures of Stöhr, to which a few original photomicrographs and some illustrations from recent textbooks have been added. The work is prefaced with a simple description of the compound microscope and directions for its use. The text is interlarded with detailed directions for the study and drawing of the prepared sections furnished. The author does not regard the study of fresh tissue as practicable for beginners. There is an appended list of titles for the student who may have been inspired to seek further information.

Grundlagen der allgemeinen und speziellen Arzneiverordnung. Von Paul Trendelenburg. Herausgegeben von Otto Krayer, Professor der Pharmakologie an der Amerikanischen Universität Beirut (Libanon). Fourth edition. Paper. Price, 16.20 marks. Pp. 322. Berlin: F. C. W. Vogel, 1938.

The first part of this book (twenty-eight pages) deals briefly with the general technic of medication, the remainder (almost 300 pages) with the special technics. In the second part are discussed with practical detail and under a therapeutic classification the technic of prescribing and administering the important medicinal substances. The author intentionally avoids all theory as well as all discussion of the nature and mode of action of the various bodies under discussion. He describes, on the other hand, in practical detail the nature of the remedies and their indications, untoward effects and dangers, as well as methods of giving them, including numerous illustrative prescriptions. In a book dealing so extensively with the administration of medicines, it is to be régretted that so little attention is paid to elegant or palatable medication.

Néphropathies et néphrites. Leçons cliniques (1934-1936). Par F. Rathery, professeur de clinique thérapeutique médicale à la Faculté de médecine de Paris. [2me série.] Paper. Price, 60 francs. Pp. 356, with 30 illustrations. Paris: Librairie J. B. Baillière et fils, 1937.

This volume is a second series of clinical lectures embracing material similar to that in the former volume by the same author. The cases presented are all interesting and for the most part unusual or frankly rare. The prolixity and repetition inherent in the presentation of clinical lectures perhaps unnecessarily lengthens some of the chapters. Nevertheless the accounts of the cases are enlivened by the engaging language of Professor Rathery. The lectures open with a discussion of classification of nephritis and the author offers what he is pleased to term a "functional" classification, wherein kidney lesions are divided into nephropathies and nephritides, the former group showing evidence clinically or pathologically of renal alteration without accompanying functional impairment while the latter group embraces renal lesions which show functional changes with or without superimposed evidences of the play of bodily compensatory mechanisms. The classification is novel but, like all others, is too circumscribed and leaves much to be desired. Case studies include purpuric nephritis, chronic azotemic and hypochloremic nephritis secondary to a unilateral renal lesion, renal acidosis, renal forms of endocarditis lenta, various types of "nephrosis," lead and mercurial nephritis, hepatonephritis, gouty kidney, nephritis secondary to lithiasis and finally renal dwarfism. The cases presented were for the most part well studied and a great many were proved at the necropsy table or from biopsy specimens procured during

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the course of surgical procedures. The author's discussion is interesting and in general accord with modern theory. Nevertheless, several of the conclusions which the author sets forth are difficult to rationalize with the stated facts in the particular case, while many of his conclusions are frankly confusing. In general the volume has reading interest for the specialist in the field of renal disease, although some of the case reviews are of such a nature as to attract internists directing their attention to metabolic or hepatic diseases.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Workmen's Compensation Acts: Rupture of Aneurysm Resulting from Strain.—Evans had not performed any manual work for four months. He was employed by the defendant to repair road scrapers, tightening bolts and boring holes with a five-eighths inch bit through 4 inch timbers. After working for twenty minutes, Evans complained of a severe pain in his abdomen and sought water and sodium bicarbonate, which he obtained at a farm house about 75 yards away. At that time he was not vomiting but "looked kind of pale as if he were in great pain," and had beads of sweat on his face. He collapsed and died within ten minutes. The physician who was called believed at first that death was due to either acute gastritis or heart trouble. An undertaker, however, in the course of embalming the body, inserted a trocar into the abdominal cavity and withdrew a quart and a half or more of blood. The physician who had been called did not learn of this until after the body had been buried, and then he concluded that death resulted from a ruptured aneurysm of the aorta, of a mesenteric artery, of the hepatic artery, or of a renal artery.

Evans' widow brought proceedings under the Idaho workmen's compensation act. The physician who had viewed the body gave his opinion as to the cause of death as stated above. Another physician, called on behalf of the widow, in response to a hypothetic question in which was given the substance of the testimony showing the symptoms presented by the deceased workman, the nature of his work immediately prior to death and the finding of blood in the abdomen, testified that Evans died of a ruptured aneurysm in the upper abdominal cavity, the rupture being due to "the increase in blood pressure due to exertion of working with the brace and bit." Another physician, however, called on behalf of the employer and his insurance carrier, testified that he had heard the testimony of the witnesses and that in his opinion the most probable cause of Evans' death was coronary disease. The cross examination of this witness indicated that in forming his opinion he did not accept the statement of the undertaker as true; he apparently did not believe the undertaker would know blood if he saw it, nor that he knew from what cavity or cavities in the body he drew it. The industrial accident board held that Evans' death was due to disease and was not the result of any injury arising out of and in the course of his employment. The district court, Oneida County, reversed the order of the industrial accident board denying compensation, and the employer and his insurance carrier appealed to the Supreme Court of Idaho.

There is no conflict, said the Supreme Court of Idaho, in the evidence in this case other than in the testimony of medical experts. The testimony of an expert as to his opinion is not evidence of a fact in dispute. It is advisory only, to assist the triers of fact to understand and apply the testimony of other witnesses. Its value depends on, among other things, the expert's confining his testimony to the facts incorporated in the question propounded to him and, if he does not assume those facts to be true and base his answer on them, his testimony is worthless and should be rejected. It is for the triers of fact to determine whether the evidence on which the expert bases his opinion is true or not. It is not for the expert to determine the truth or falsity—the reliability or unreliability—of the testimony of other witnesses. For that reason he should not be asked to base his opinion on the testimony of other witnesses which he has heard, but the facts which that testimony tends to establish and which is relied on by the party propounding the question should be hypothetically stated. The testimony of the expert should be responsive to that hypothetic question and it is his duty to assume facts embraced in the hypothetic question to be true.

The court accordingly concluded that the testimony of the physician called by the employer that the most probable cause of Evans' death was a coronary disease and that he did not hear any evidence presented in the case that would indicate to him that death resulted from a ruptured aneurysm was not entitled to be given weight and should be rejected. That testimony being eliminated, continued the Supreme Court, the remaining evidence was amply sufficient to establish that Evans died from a ruptured aneurysm due to increased blood pressure caused by the exertion required by the performance of the duties of his employment and his widow was entitled to compensation.—*Evans v. Cavanagh (Idaho), 73 P. (2d) 83.*

Taxes: Credit Association Composed in Part of Physicians Not Exempt from Taxation.—The Retailers Credit Association, a corporation organized under the laws of California, included in its membership physicians, dentists and other professional men. Among its various activities, it furnished reports on the credit rating of individuals to members, for which service a fee was charged. It also acted as a collection agency for members, receiving a commission for so doing. Its activities normally resulted in a profit and, while the by-laws provided for the payment of dividends to members under certain circumstances, no such payment had ever been made.

For the year 1931 the corporation had a net profit of $6,000. It claimed exemption from the payment of federal income taxes for that year on the ground that it was a business league within the meaning of the Revenue Act of 1928, which exempted "business leagues . . . not organized for profit and no part of the net earnings of which inures to the benefit of any private shareholder or individual." A denial of the claim for exemption was affirmed by the board of tax appeals (33 B. T. A. 1166), and the corporation appealed to the circuit court of appeals, ninth circuit.

Under the federal income tax regulations, said the court, a business league to be exempt must not engage in a regular business of a kind ordinarily carried on for profit. While the court thought that the Retailers Credit Association was a "business league" within the meaning of the income tax law, it seemed clear that one of its purposes was to engage in a regular business of a kind ordinarily carried on for profit, namely, the credit reporting aspect of its service and its collection activities, and that these activities were not incidental to the main purposes of the corporation but were primary purposes. The court therefore affirmed the ruling of the board of tax appeals denying exemption to the corporation.—*Retailers Credit Assn. of Alameda County v. Commissioner of Internal Revenue, 90 F. (2d) 47.*

Society Proceedings

COMING MEETINGS

American Urological Association, Quebec, Canada, June 27-30. Dr. Clyde L. Deming, 789 Howard Ave., New Haven, Conn., Secretary.
Maine Medical Association, Bar Harbor, June 26-28. Dr. F. R. Carter, 22 Arsenal St., Portland, Secretary.
Medical Library Association, Boston, June 28-30. Miss Janet Doe, 2 East 103d St., New York, Secretary.
Minnesota State Medical Association, Duluth, June 29-July 1. Dr. E. A. Meyerding, 11 West Summit Ave., St. Paul, Secretary.
National Medical Association, Hampton, Va., Aug. 15-19. Dr. John T. Givens, 1108 Church St., Norfolk, Va., General Secretary.
West Virginia State Medical Association, White Sulphur Springs, July 11-13. Mr. Joe W. Savage, Public Library Building, Charleston, Executive Secretary.
Wyoming State Medical Society, Laramie, Aug. 7-9. Dr. M. C. Keith, 156 South Center St., Casper, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers in continental United States and Canada for a period of three days. Periodicals are available from 1927 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them. Titles marked with an asterisk (*) are abstracted below.

American Journal of Anatomy, Philadelphia

62: 427-522 (May) 1938

Growth, Desquamation and Involution of Vaginal Epithelium of Fetuses and Children, with Consideration of Related Hormone Factors. L. Fraenkel and G. N. Papanicolaou, New York.—p. 427.

Quantitative Study of Lymphoid Organs of Albino Rat. J. E. Kindred, Charlottesville, Va.—p. 453.

Microscopic Changes in Hypophysis of Albino Rat Following Exposure to Cold, and Their Relationship to Physiology of Secretion. R. N. Baillif, New Orleans.—p. 475.

Study of White Blood Cells of the Normal Guinea Pig. A. L. Joyner, New York.—p. 497.

Number and Size of Mammalian Glomeruli as Related to Kidney and to Body Weight, with Methods for Their Enumeration and Measurement. D. A. Rytand, San Francisco.—p. 507.

American J. Digestive Diseases, Huntington, Ind.

5: 153-216 (May) 1938

Amebic Dysentery in North Carolina. J. M. Ruffin, Durham, N. C.—p. 153.

Proctologic Aspects of Diarrhea. G. W. Ault, Washington, D. C.—p. 155.

Importance of Recognizing Contracted Anus. L. A. Buie and W. L. Butsch, Rochester, Minn.—p. 162.

Effect of Aluminum Hydroxide Cream on Absorption from Gastrointestinal Tract. J. M. Beazell, C. R. Schmidt and A. C. Ivy, Chicago.—p. 164.

History of Development of Stomach Tube with Some Notes on Duodenal Tube. J. Friedenwald and S. Morrison, Baltimore.—p. 165.

Therapeutic Application of Acidophilus Milk in Constipation of Children. L. F. Rettger, L. Weinstein, M. Bogin and J. E. Weiss, New Haven, Conn.—p. 170.

Benign Ulcer of Gallbladder. A. C. van Ravenswaay, Boonville, Mo.—p. 173.

Peptic Esophagitis: Case. Frances R. Vanzant, L. Daily and J. R. Phillips, Houston, Texas.—p. 175.

Preplacing Bacillus Coli by Bacillus Paratyphosus B in Large Intestines in Guinea Pigs. Dorothy K. O'Connor, L. Arnold and H. E. McDaniels, Chicago.—p. 176.

*Nutritional Value of Soybeans. A. A. Horvath, Newark, Del.—p. 177.

Blood Diastase in Hepatic and Biliary Disease. M. Rachmilewitz, Jerusalem, Palestine.—p. 184.

Quantitative Studies on Case of Migraine. R. Fainer, Haifa, Palestine.—p. 189.

Nutritional Value of Soybeans.—Horvath reviews the work done on the nutritive value of soybeans, enumerates the mineral constituents and their disease-protective properties and points out the relative low cost of soybean products. As an economic source of valuable and wholesome dietary elements the soybean probably has no peer. The presence of phosphatides in soybeans may have some special physiologic value because phospholipoids are constituents of all the body cells, the nervous tissue being particularly rich in phosphatides. In 1936 a protective factor against nutritional encephalomalacia of chicks was discovered in the nonsaponifiable fraction of certain edible oils, which are headed by soybean oil. It has been found by Miller and Robbins that, compared with most vegetables, soybeans have unusually large amounts of protein, fat, calcium, phosphorus and iron. Cooked immature soybeans proved to be a good source of vitamins A, B and G and a poor source of vitamin C. Besides bread and bakery products the other main outlets for soya flour are for the manufacture of crackers, pancake flour, cocoa-malt mixes, baby foods, chocolate, puddings, ice cream powders, macaroni products and sausages. The addition of soya flour renders these products more nutritious and palatable. The Food Research Division of the United States Department of Agriculture has stated that the most expensive food constituents are minerals, vitamins, proteins and fats. Soybean flour is rich in all these food constituents and yet relatively cheap. The moderate cost of soybean flour makes it possible for people of small incomes to obtain the maximum of these essential nutritional constituents required by the body, which in the form of other foods might be beyond their reach.

American Journal of Surgery, New York

40: 321-502 (May) 1938

Renal Rickets or Renal Dwarfism. T. L. Howard, Denver.—p. 323.

Difficulties in Urethral Catheterization. J. L. Emmett, Rochester, Minn.—p. 349.

*Traumatic Lesions of Kidney. J. T. Priestley and F. Pilcher Jr., Rochester, Minn.—p. 357.

Measurement of Kidney Function Before, During and After Pregnancy. A. W. Holman, Portland, Ore.—p. 365.

Transperitoneal Exclusion Cesarean Section Through Lower Uterine Segment. I. F. Frost, New York.—p. 370.

Intravenous Anesthesia in Obstetrics: Comparative Study of Pentothal and Evipal Soluble with Report of 250 Cases. F. A. Kassebohm and M. J. Schreiber, New York.—p. 377.

Surgical Treatment of Syringomyelia. L. J. Adelstein, Los Angeles.—p. 384.

Common Duct Obstruction. W. S. Sargent, San Diego, Calif.—p. 396.

High Ligation of Cystic Vessels in Subserous Cholecystectomy: Use of Silver Clips. L. R. Whitaker, Portsmouth, N. H.—p. 407.

Enterogenous Cysts. B. Sherwin, New York.—p. 413.

*Carbuncle. J. K. Berman, Indianapolis.—p. 419.

Physiologic Basis for Ligation of Great Saphenous Vein in Treatment of Varicose Veins. J. R. Veal and B. D. Van Werden, New Orleans.—p. 426.

Rationale of Surgical Technic in Carcinoma of Rectum and Sigmoid. J. M. Lynch and G. J. Hamilton, New York.—p. 432.

Electrosurgery in Proctology. R. V. Gorsch, New York.—p. 436.

Low Back Pain. A. J. Buka, Pittsburgh.—p. 444.

Fractures of the Hip Joint. F. Mogavero, Philadelphia.—p. 447.

Femoral Herniorrhaphy. S. J. Burrows, Chicago.—p. 451.

Traumatic Lesions of Kidney.—From 1910 to 1933 Priestley and Pilcher encountered forty-five cases in which they made the diagnosis of rupture of the kidney by external trauma without penetration of the skin. Twenty-four of the patients were seen immediately or within one week following injury, eleven were first seen from one week to one month after the initial injury and the remaining ten patients were first seen from one month to several years or more after injury. The type of renal injury varied from slight subcapsular hemorrhage to complete pulpefaction of the kidney. In some cases the ureter or renal pedicle was completely avulsed. Hemorrhage, usually perirenal but occasionally intraperitoneal, was uniformly present and hematuria, either gross or microscopic, occurred in 95 per cent of the cases. Leakage of the urine around the kidney was common. Serious associated injuries elsewhere in the body were present in 13.3 per cent of cases. Healing may occur satisfactorily with medical treatment, or on the other hand urinary fistulas, hydronephrosis, pseudohydronephrosis, pyelonephritis or anatomic abnormalities of varying degrees may persist or develop. A history of trauma and hemorrhage and pain are cardinal points in the diagnosis, but they should also be substantiated by intravenous urography. In general, medical treatment immediately following the injury is preferred unless contraindicated. Subsequent operation may become necessary in some cases. The two deaths that occurred in the series were attributed to severe extrarenal trauma. Thirty-one patients were followed for a period of from four to twenty-six years subsequent to injury. Eleven patients who underwent nephrectomy are entirely free of symptoms; 73.7 per cent of those treated medically are entirely well and the remainder of the group have mild symptoms referable to the urinary tract.

Carbuncle.—Berman believes that a study of the microscopic anatomy of the skin on the back of the neck and on the face clearly explains the behavior of carbuncle and definitely establishes carbuncle of the face as a distinct entity. He studied 125 cases of severe carbuncle, eighty-three in men and forty-two in women. The majority occurred on the back of the neck in both men and women, but carbuncle occurred twice as commonly on the face of women, whereas it was more common on the scalp of men. The face is a dangerous place, for four of the nine deaths occurred in facial carbuncle. Most carbuncles occurred in patients without debilitating disease; this was more noticeable in women than in men. Obviously the "picking" of cutaneous infections is an important causative factor. Of all associated diseases, diabetes is most frequent.

Carbuncle of the face should be treated conservatively. The general mortality in facial carbuncle was 40 per cent. Carbuncle elsewhere on the body, associated with severe debilitating disease, must also be treated conservatively. Five of the nine deaths occurred in this group. The general mortality was 18 per cent. Carbuncle not on the face and not associated with severe disease should be treated by surgical intervention. This may be by excision or incision. The general mortality in this group was 1 per cent.

Journal of Biological Chemistry, Baltimore

123: 375-612 (April) 1938. Partial Index

Buffer Action of Unidentified Urine Constituents. A. C. Kuyper, Columbus, Ohio.—p. 409.
Surface Denaturation of Egg Albumin. H. Wu and C.-F. Wang, Peiping, China.—p. 439.
Carbohydrate Metabolism of Brain: VI. Isolation of Glycogen. S. E. Kerr, Beirut, Lebanon.—p. 443.
Hydrogen Ion Concentration Stability of Papilloma Virus Protein. J. W. Beard and R. W. G. Wyckoff, Princeton, N. J.—p. 461.
Biologic Assay of Carbohydrate Metabolism Hormone of Anterior Pituitary. A. J. Bergman and C. W. Turner, with technical assistance of P. T. Cupps, Columbia, Mo.—p. 471.
Differential Migration of Pressor and Oxytocic Hormones in Electrophoretic Studies of Untreated Press-Juice of Posterior Lobe of Pituitary Gland. G. W. Irving Jr. and V. du Vigneaud, Washington, D. C.—p. 485.
Interaction of Vitamin B_1 in Enzymic Reactions. H. Tauber, Florence, S. C.—p. 499.
Intermediate Forms of Oxidation-Reduction of Flavins. L. Michaelis and G. Schwarzenbach, New York.—p. 527.
Properties of Hemoglobin and Pepsin in Solutions of Urea and Other Amides. J. Steinhardt, Boston.—p. 543.
Radioactive Phosphorus as an Indicator of Phospholipid Metabolism: II. Role of Stomach, Small Intestine and Large Intestine in Phospholipid Metabolism in Presence and Absence of Ingested Fat. B. A. Fries, S. Ruben, I. Perlman and I. L. Chaikoff, Berkeley, Calif.—p. 587.

Journal of Comparative Neurology, Philadelphia

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Efferent Connections of Flocculonodular Lobe in Macaca Mulatta. R. S. Dow, New Haven, Conn.—p. 297.
Relations of Fascia Dentata, Hippocampus and Neocortex and the Nature of the Subiculum. A. A. Abbie, Sydney, Australia.—p. 307.
Study of Nissl Pattern in Motor Cells of the Hindbrain of Lizard (Tackydromus Septentrionalis) Under Various Conditions. Wei Chen Chow, Nanking, China.—p. 335.
Studies on Developing Behavior of Anura. K. A. Youngstrom, Lawrence-Kansas City, Kan.—p. 351.
Prenatal Growth of Cat: VII. Growth of the Brain and of Its Parts, of the Spinal Cord and of the Eyeballs. H. B. Latimer, Lawrence-Kansas City, Kan.—p. 381.
The Weights of the Brain and of Its Parts, of the Spinal Cord and of the Eyeballs in the Adult Cat. H. B. Latimer, Lawrence-Kansas City, Kan.—p. 395.

Journal of Nervous and Mental Disease, New York

87: 545-676 (May) 1938

Is There a Relative Increase in Mental Disease? B. Malzberg, Albany, N. Y.—p. 545.
Blood Pressure and Pulse Rate in Prison Psychosis. R. Schwarz, Dannemora, N. Y.—p. 556.
*Insulin in Treatment of Acute Mania. L. C. Grosh Jr., Ypsilanti, Mich.—p. 559.
*Effect of Induced Metrazol Convulsions on Schizophrenic Patients. H. H. Reese, Madison, Wis.; A. H. Vander Veer, Chicago, and A. H. Wedge, Mendota, Wis.—p. 570.
Psychologic Effect of Benzedrine Sulfate. P. Schilder, New York.—p. 584.
Correlations of Athetosis, Catatonia and Hypoglycemia. K. Gyárfás, Budapest, Hungary.—p. 588.
Electroencephalography in Diagnosis and Localization of Intracranial Conditions. T. J. Case, Chicago.—p. 598.

Insulin in Treatment of Acute Mania.—Grosh states that recently at the Ypsilanti State Hospital three cases have been observed of apparent diabetes mellitus occurring during the course of the manic phase of manic-depressive psychoses. Two of the cases referred to were studied not only during the periods of acute elation but also during lucid intervals of more normal activity. The study of the dextrose tolerance curves taken during these two periods demonstrates that, while in neither period are they consistently grossly abnormal, still there is a distinct prolongation of the blood sugar elevation during the elated period when compared to the curves obtained under normal conditions, which are suggestive of increased tolerance. This comparison suggested that there was some relative loss of tolerance during the attack for which insulin might be used in a remedial role. In both of these cases it might possibly have been mere coincidence that the psychomotor activity was sharply cut down to the normal level after a few days of insulin therapy. None the less this type of therapy is suggested as a reasonable procedure in the acute elations in which the dextrose tolerance test reveals a relatively high type of curve when compared with the curve in normal activity.

Metrazol Convulsions in Schizophrenia.—Reese and his co-workers have been using metrazol since February 1937 in the treatment of forty-one cases of schizophrenia. Twenty patients have finished their treatment, while twenty-one others are still under treatment. A 10 per cent aqueous solution prepared from the solid drug, placed in 50 cc. rubber-capped vials and sterilized in an open sterilizer at 100 C. for thirty minutes, is employed. Of the twenty patients in whom metrazol treatment has been completed, four have been discharged in full remission, six are improved and ten have not been benefited. In observing these patients the authors have always kept in mind a comparison with insulin shock therapy. The two forms of therapy differ in many ways, despite their common goal of rendering the patient unconscious. With metrazol, if improvement is to occur, it generally appears quickly and proceeds in spurts; with insulin, improvement is slow and steady. Patients treated with insulin always exhibit their first lucid intervals in immediate relation to hypoglycemia, while those given metrazol do not show improvement until the first or second day after treatment. Stuporous catatonic patients do not respond well to insulin; however, they furnish the most suitable subjects for metrazol therapy. Patients in whom symptoms are of more than a year's duration show little or no improvement when treated with insulin; the status of such patients when they are given metrazol, however, may change considerably for the better, even though full recovery does not take place. A judicious combination of the two methods often seems to produce the best results.

Kentucky Medical Journal, Bowling Green

36: 167-208 (May) 1938

Public Health the Basic Factor of Social Security. A. T. McCormack, Louisville.—p. 171.
Influenza. W. Dean, Louisville.—p. 178.
*The Management of Acute Diarrheas of Infancy. M. C. Spradlin, Somerset.—p. 181.
Pelvic Infections. I. J. Hoover, Owensboro.—p. 185.
Some Practical Considerations in Diagnosis and Treatment of Syphilis. A. B. Loveman, Louisville.—p. 189.
Nephritis in Childhood. J. W. Bruce, Louisville.—p. 196.
Urolithiasis. E. D. Smith, Owensboro.—p. 199.
Better Obstetrics and Less Gynecology. E. C. Wilhite, Covington.—p. 202.

Acute Diarrheas of Infancy.—Spradlin states that the prophylaxis of diarrhea resolves itself into the following measures: (1) prevention of the infant from becoming overheated, (2) pure, uncontaminated water, (3) intelligent conservative diet, (4) cautious, gradual introduction of new foods to the infant, (5) adequate refrigeration of the baby's food, (6) screening to prevent bacterial contamination by flies and (7) prevention of parenteral infection by avoiding colds and their prompt treatment when they occur. When an acute diarrhea does occur the child should be kept at absolute rest. If necessary, adequate rest should be secured by the use of sedatives. In early, relatively nontoxic cases, adequate fluids (maximum 15 cc. per pound of body weight) may be given by mouth. In the more severe cases the use of one or more transfusions, at intervals of from twenty-four to forty-eight hours, with cross-matched citrated blood is a life saving measure. When parenteral infections are found, the clearing up of these infections is essential to the cure of the diarrhea. Proper dietary management is secondary only to the maintenance of a satisfactory water balance and elimination of any parenteral infection. All patients should have a preliminary starvation period during which only fluids are given. This period may vary from eight to forty-eight hours or even longer, depending on the severity and duration of the case. At the end of this period, in all types but the putrefactive diarrheas, breast milk or the basic milk mixture, if of sound composition, may be resumed in markedly reduced quantities. As the diarrhea gets under control, the amount of the milk mixture may be increased gradually up to the normal requirement. In the proteolytic or fermen-

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tative diarrheas the most rational treatment is the administration of an 8 per cent preparation of maltose and dextrin or corn syrup solution after the initial starvation period. This is followed after twenty-four hours by the use of thin cereal gruels for several days before dilute milk mixtures are resumed. The raw apple diet and methods based on it hold great promise of supplanting the older, more conventional methods of treating diarrhea. Saline or sodium bicarbonate colonic irrigations are of particular value when the fever is high or when there is much cramping. These may be followed by a thin starch solution as a retention enema. The following drugs merit consideration: purgatives, opium, bismuth, sedatives, stimulants, atropine, calcium gluconate, alkalis and specific drugs such as emetine, carbarsone, vioform or other antiamebic drugs.

Medical Annals of District of Columbia, Washington

7: 107-136 (April) 1938

Some Erroneous Concepts Encountered in the Practice of Gastroenterology. J. L. Kantor, New York.—p. 107.
Surgical Treatment of Peptic Ulcer. C. S. White, Washington.—p. 114.
Clinical Observations on Rectal Digitalis Therapy in Congestive Heart Failure. J. S. Diasio, New York.—p. 118.
Nutritional Standards for Normal Growth. J. M. Moser, Washington.—p. 121.
Management of Vesical Paralysis. N. Belt, Washington.—p. 125.

Missouri State Medical Assn. Journal, St. Louis

35: 159-196 (May) 1938

Diagnosis and Treatment of Hypertrophic Arthritis. J. A. Key, H. J. Rosenfeld and O. E. Tjoflat, St. Louis.—p. 159.
*Newer Treatment of Arthritis and Similar Conditions. J. J. Bredall, Perryville.—p. 164.
Insulin Shock Therapy: Its Importance in General Practice. G. W. Robinson Jr., Kansas City.—p. 168.
Rickets and Osteomalacia. I. B. Horowitz, St. Louis.—p. 169.
Acute Hemolytic Anemia Following Treatment with Sulfanilamide. A. M. Ginsberg and J. B. Brams, Kansas City.—p. 174.
Sulfanilamide in Treatment of Puerperal Septicemia. E. G. Cope, Hornersville.—p. 174.
Public Health: The Truth. J. F. Chandler, Oregon.—p. 175.
Unusual Case of Fistula in Ano. J. S. Poe, St. Louis.—p. 178.

Iontophoresis in Arthritis.—Bredall describes the treatment of arthritis by iontophoresis or ionization with the simple galvanic machine using acetyl-beta-methylcholine chloride. A 0.1 per cent or a 1:1,000 solution of the drug is introduced into the affected part from the positive electrode. Absorbent paper, sheet wadding, reinforced asbestos fabric paper or cotton filled bandage is saturated with the solution and wrapped round the part to be treated. On top of this a tin lead plate or strip is wrapped around the part and connected with the positive pole of the galvanic machine. A large regular moist pad electrode is placed under the back or over the abdomen and connected with the negative pole. The current is gradually increased to from 20 to 30 milliamperes and maintained for from twenty to thirty minutes. Then the current is slowly turned off, the electrodes are removed, and the parts are dried and wrapped. There may be a slight tingling sensation under the electrodes during the treatment but the strength of the current must always be within comfortable toleration of the patient. Iontophoresis is contraindicated in septic conditions and in bronchial and other types of asthma, and it must be used with caution in patients with a cardiac involvement. There was definite improvement in sixteen of twenty patients. Most of these patients have previously had a long trial of treatment with conventional methods without results. Many patients showed not only definite elimination of swelling and deformity but also improvement in strength and function.

New England Journal of Medicine, Boston

218: 711-748 (April 28) 1938

Studies on Familial Aspects of Cancer. H. L. Lombard, Boston.—p. 711.
*Peritoneoscopy. E. B. Benedict, Boston.—p. 713.
Condition of Cervix as Determined by Vaginal Examination: True Index of End of Pregnancy. R. S. Titus, Boston.—p. 720.
Gout: Report of Unusual Case in a Woman. J. A. Halsted, Dedham, Mass.—p. 723.

Peritoneoscopy.—Benedict has made forty-eight examinations with the Ruddock peritoneoscope. There has been one fatality, in which pneumoperitoneum may well be considered as a contributory cause of death. The patient was in the terminal stages of multiple lung abscess, coronary disease and possible echinococcic cyst of the liver. An error in judgment was made in subjecting him to the stress and strain of sedative drugs and peritoneoscopy. There have been no other complications except a subcutaneous emphysema in a few cases. No real errors in diagnosis have occurred. When patients are carefully selected, peritoneoscopy is attended with little risk. Those with serious pulmonary or cardiac disease are not good prospects. Abdominal adhesions may complicate the procedure, but by careful selection of the site of puncture difficulties have thus far been avoided. Peritoneoscopy may be indicated in any abdominal or pelvic condition in which the diagnosis is obscure or in which additional evidence is needed to confirm a diagnosis or to plan treatment. The procedure will frequently give information that will decide for or against laparotomy. Peritoneoscopy is useful in cancer, cirrhosis, tuberculous peritonitis, ascites, pelvic tumors, ectopic pregnancy and ovarian dysfunction. In one case an excellent view was obtained of a polycystic liver, in another case of supposed echinococcic cyst the liver was found to be normal, and in a third case in which there was a questionable palpable mass the peritoneal cavity was found to be normal. Serious cardiac or pulmonary disease may be a contraindication, for the peritoneal distention necessary for a satisfactory examination may somewhat embarrass the circulation and the diaphragmatic movements. Because of the danger of spreading infection, peritoneoscopy is contraindicated in inflammatory conditions. Peritoneoscopy will not replace exploratory laparotomy in all cases, but in certain cases it makes it possible to avoid major surgical operations. Peritoneoscopy requires local anesthesia, a stab incision and hospitalization of one day.

New Orleans Medical and Surgical Journal

90: 639-696 (May) 1938

Factors Influencing the Development of Tuberculosis. F. H. Heise, Trudeau, N. Y.—p. 639.
Undulant Fever with Endocarditis and Mycotic Aneurysm: Case Report. J. E. Knighton Jr., Shreveport, La.—p. 646.
Report of the Pasteur Institute of Charity Hospital of Louisiana at New Orleans for the Year 1937. R. D'Aunoy and J. H. Connell, New Orleans.—p. 648.
History of Cesarean Section. J. W. Reddoch, New Orleans.—p. 650.
Anatomic Consideration of Dystocia. H. Cummins, New Orleans.—p. 652.
Indications for Cesarean Section. W. E. Levy, New Orleans.—p. 652.
Contraindications for Cesarean Section. M. L. Stadiem, New Orleans.—p. 654.
Choice of Operation in Cesarean Section. P. Graffagnino, New Orleans.—p. 655.
Adequate Medical Care. E. L. Sanderson, Shreveport, La.—p. 656.
Social Security and Public Welfare: Relation of the Medical Social Worker to the Physician. Beatrice Hodge, New Orleans.—p. 659.
Some Phases of the Social Security Act. Elizabeth Wisner, New Orleans.—p. 662.
The State Hospital and Welfare Boards. O. P. Daly, Lafayette, La.—p. 664.
Federal and State Program for Maternal and Child Health. R. W. Todd, New Orleans.—p. 668.
Relation Between Preventive Medicine and Federal and State Welfare Programs. W. H. Perkins, New Orleans.—p. 670.

Oklahoma State Medical Assn. Journal, McAlester

31: 107-152 (April) 1938

Congenital Visceral Anomalies as Exemplified by Developing Vascular System. C. F. De Garis, Oklahoma City.—p. 107.
*Chronic Arthritis and Undulant Fever: Their Interrelationship. E. Goldfain, Oklahoma City.—p. 111.
Consideration of the Varied Symptomatology of Prostate and Verumontanum. A. R. Russell, McAlester.—p. 114.
Endocrinology: Its Practical Application in Gynecology. P. N. Charbonnet and E. O. Johnson, Tulsa.—p. 116.
Relative Value of Various Methods of Diphtheria Immunization. C. E. Bradley, Tulsa.—p. 124.
Further Experience with Prostatic Resection. H. S. Browne, Tulsa.—p. 126.

Chronic Arthritis and Undulant Fever.—Goldfain declares that the ambulatory and especially the chronic or subclinical cases of brucellosis in man should be of interest to the physician who would study carefully any case giving a history of rheumatic or arthritic symptoms. The symptoms of subclinical or chronic types of brucellosis (arthralgia, arthritis, headache, backache, malaise, weakness, neuritis or neuralgia, myositis, leukopenia, secondary anemia, spondylitis and persistent joint stiffness), in their entirety or in part, may well lead to a diagnosis of chronic rheumatic disease or chronic arthritis without brucel-

losis ever being suspected unless it is tested for properly. It has been quite definitely proved that the agglutination test may be negative in at least 5 per cent of the cases. Other diagnostic measures therefore must be used to determine its presence. These are the opsonocytophagic test and the cutaneous test.

Rocky Mountain Medical Journal, Denver

35: 345-424 (May) 1938

*Parasitic and Infectious Diseases Transmitted Through Meat and Dairy Products. G. H. Koon, San Antonio, Texas.—p. 362.
Differentiation of Various Types of Enterocolitis and Their Management. J. A. Bargen, Rochester, Minn.—p. 370.
Medical Management of Peptic Ulcer. R. H. Finney, Pueblo, Colo.—p. 374.
Surgical Aspects of Peptic Ulcer. G. E. Rice, Pueblo, Colo.—p. 376.
Profuse Hemorrhage in Peptic Ulcer. B. E. Konwaler, Pueblo, Colo.—p. 378.
Value of Papaverine Hydrochloride in Treatment of Postoperative Pulmonary Embolism. D. C. Collins, Los Angeles.—p. 381.
It's a Fact. Mary B. Miller, Pittsburgh.—p. 386.

Diseases from Meat and Dairy Products.—The diseases most frequently caused by contaminated foods are those of the intestinal group. These Koon lists as typhoid and paratyphoid fever, common diarrhea, bacillary dysentery, protozoal dysentery, cholera, helminthic infestations, undulant fever, food infection and food intoxication. Diseases other than those belonging to the intestinal group, such as septic sore throat, diphtheria, scarlet fever or tuberculosis, may be transmitted by food but, except in the case of septic sore throat, food constitutes merely an incidental and not the usual or principal agency of transmission. Flesh of animals suffering from diseases due to the Gärtner group of organisms, such as septicemia and diarrhea, or from puerperal fever or tuberculosis may serve to transmit pathogenic organisms to the consumer. Human infection with animal parasites, introduced through the medium of food, is of special interest because of the number of helminths and protozoa which pass all or part of their lives in the intestine. The only consequential source of trichinosis for man exists in hogs, although a variety of other animals may be infested. Infestation of swine can be controlled by a swine sanitation system. The campaign to educate the public against the use of any raw or partially cooked pork should be better organized and more intensive. There are several tapeworms (beef, swine and fish) which man shares with the lower animals. The most frequent form of food poisoning in man is caused by foods infested with members of the Salmonella (paratyphoid enteritidis) group or with other bacteria, especially the staphylococci. Of the foods involved, meat products are only slightly more frequently involved than nonflesh foods (68 per cent). Practicing physicians and those engaged in public health work can contribute largely to the epidemiologic control of disease by interesting themselves in and lending their efforts to securing local or state laws governing food inspection that are comparable to the federal meat inspection act. Such activities should be removed from the influence of local or state politics.

Southwestern Medicine, El Paso, Texas

22: 165-208 (May) 1938

Medical Progress and Its Significance. H. W. Rice, Bisbee, Ariz.—p. 165.
Treatment of Tuberculosis of Upper Extremity. A. Steindler, Iowa City.—p. 168.
Tumors of the Breast. G. W. Jones, Philadelphia.—p. 172.
Laryngotracheobronchitis. P. H. Holinger and A. H. Andrews Jr., Chicago.—p. 174.
First Aid Mindedness in Treatment of Fractures. C. E. Yount, Prescott, Ariz.—p. 178.
Upper Respiratory Infection from Spirochaeta Bronchialis in Children. R. D. Haire, Hobbs, N. M.—p. 181.
Sinus Thrombosis and Mastoiditis Without Otorrhea. J. H. Childrey, San Francisco.—p. 182.

Wisconsin Medical Journal, Madison

37: 361-444 (May) 1938

Treatment of Diseases of the Heart. F. A. Willius, Rochester, Minn.—p. 377.
Stabilization of Mandibular Joint by Injection of Sclerosing Solution. R. P. Gingrass, Milwaukee.—p. 383.
Treatment of Acute Mastoiditis. J. K. Trumbo, Wausau.—p. 385.
Prophylaxis and Therapy of Eclampsia. J. B. Vedder, Marshfield.—p. 394.
Meningitis Caused by Bacillus Influenzae: Report of Case. H. A. Bachhuber, Sauk City.—p. 399.
Staphylococcic Conjunctivitis. C. S. O'Brien, Iowa City.—p. 401.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Children's Diseases, London

35: 1-84 (Jan.-March) 1938

Gaucher's Disease in Children. F. R. B. Atkinson.—p. 1.
Anomalous Forms of Varicella. G. W. Ronaldson and W. H. Kelleher.—p. 22.
Clinical Anatomy of Cases of Epispadias and Extroversion of the Bladder. A. R. Thompson.—p. 36.

Journal of Tropical Medicine and Hygiene, London

41: 125-140 (April 16) 1938

Third Note on Infectivity to Man of Strain of Trypanosoma Rhodesiense: Two Further Passages Through Antelopes and Tests on Volunteers. J. F. Corson.—p. 125.
*Multiple Myeloma with Hyperglobulinemia. G. M. Decherd Jr. and L. Holland.—p. 129.

Multiple Myeloma with Hyperglobulinemia.—Decherd and Holland cite two cases of multiple myeloma which illustrate the highly variable clinical picture that this condition may present. The first patient showed an anemia, hypercalcemia and hyperglobulinemia, with a greatly accelerated sedimentation rate. Bence Jones protein was excreted in large amounts. There were probably extensive pulmonary metastases. The second patient was thought to have chronic arthritis on admission, but the pain in the chest and back was due to skeletal involvement by myeloma. There was nitrogen retention in the blood, without an elevation of blood pressure and a high serum calcium with normal phosphorus. An increase in blood proteins is uncommon and, when found, should lead one to suspect multiple myeloma. Myeloma should be considered in all atypical cases of renal disease showing nitrogen retention without hypertension. Renal involvement is found in approximately 70 per cent of cases, ranging from proteinuria alone to renal insufficiency. Bence Jones protein is found in approximately half of the cases of multiple myeloma, and its presence is strongly suggestive of this disease. However, other conditions may lead to the renal excretion of this protein, notably diseases involving the bone marrow, such as leukemia or metastatic carcinomatosis, or chronic accumulation of pus, as in empyema.

Medical Journal of Australia, Sydney

1: 639-682 (April 9) 1938

*Bacteriologic and Clinical Study of Professional Personnel of Maternity Hospitals, with Special Reference to Carriers of Hemolytic Streptococci. Lucy M. Bryce and Phyllis Tewsley.—p. 639.
Further Observations on Delayed Testis. A. B. McCutcheon.—p. 654.
Traumatic Rupture of Urethra and Its Treatment. H. Moore.—p. 657.
The Turbulent Dr. Lhotzky. J. MacPherson.—p. 661.

Personnel of Maternity Hospitals.—Bryce and Tewsley discuss an outbreak of three cases of puerperal fever and the measures adopted to deal with it and those designed to prevent future similar outbreaks. In addition to the recognized biochemical and serologic methods of classification of hemolytic streptococci, their sensitivity to four serologically distinct types of streptococcus bacteriophage was tested; it was not found to be in complete agreement with the results of the precipitin test. The variation of sensitivity to bacteriophage among strains falling into Lancefield's group A suggests, however, that this property might be used in epidemiologic studies. The incidence of throat carriers of group A streptococci among the contacts of the three patients with puerperal fever was found to be 22 per cent. On two subsequent occasions, when there had not been recent known contact with streptococcic infections, the incidence of group A streptococci among similar groups of medical practitioners and nurses was respectively 3 and 6.7 per cent. In persons with healthy respiratory tracts the presence of hemolytic streptococci in throat swabs appeared to be closely associated with recent contact with streptococcic illness. In the personnel with clinically detectable abnormality of the nasopharynx there was a greater tendency to harbor hemolytic streptococci irrespective of recent contact. Exclusion from maternity units of persons with such abnormality, by means of preliminary medical examination, would be a possible way of reducing the risk of infection of patients and the disorganization attendant on their withdrawal during a period of obstetric work.

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Presse Médicale, Paris

46: 697-712 (April 30) 1938

*Urea Clearance Test (Coefficient of Van Slyke) in Study of Renal Function. Pasteur Vallery-Radot, P. Delafontaine and J.-F. Porge.—p. 697.

Shortening of the Mean Delay Between the Age of Primary Tuberculous Infection and the Age of Pulmonary Tuberculosis as a Disease: Practical Consequences. E. Bernard and J. Weil.—p. 698.

Urea Clearance Test (Van Slyke) and Renal Function.—Pasteur Vallery-Radot and his collaborators, after calling attention to Ambard's laws on the concentration of urea in the urine and in the blood, review the studies of American authors on the excretion of the urea in the volume of urine, citing Van Slyke's formulas for the maximal clearance and for the standard clearance of urea. The formula for the maximal clearance is applied if the volume of urinary secretion is equal or superior to 2 cc. per minute; that for the standard clearance is employed when the urinary secretion is below 2 cc. per minute. The authors made comparative studies with Ambard's constant and with Van Slyke's formula for urea clearance on sixty-one patients. In forty-six (75 per cent) the tests of Ambard and Van Slyke produced comparable results. Eleven of these forty-six subjects were free from renal disturbances according to the tests, whereas the thirty-five others had manifest renal insufficiency. In fifteen subjects (25 per cent) the tests of Ambard and of Van Slyke gave discordant results. In one case the test of Van Slyke was abnormal, while the constant of Ambard and the other functional tests gave normal results. In fourteen other cases, Van Slyke's test was normal when Ambard's disclosed increased values; in ten of these subjects the other renal tests gave normal results. The authors say that it cannot be concluded from this that one test is more sensitive than the other, for the two tests estimate the urea secretion on a different basis. They think that the urea clearance test of Van Slyke has a place among the other renal tests. It is simple and gives evidence of the renal "flexibility." This functional flexibility of the normal kidney is opposed to the functional rigidity of the diseased kidney. A number of investigators have accepted this idea as fundamental.

46: 729-752 (May 7) 1938

Slow and Continuous Injection of Insulin in Diabetic Patients: Insulin Requirements, Maintenance Dose, Dissociated Action on Glycosuria and Acetonemia. A. Baudouin, J. Lewin and E. Azérad.—p. 729.

Inflammatory Exacerbations in Course of Pulmonary Tuberculosis. R. Benda and H. Mollard.—p. 732.

*Study of Exchange of Vitamin C of Mother and Nursing Infant. W. Neuweiler and J. Hubscher.—p. 734.

Vitamin C in Mother and Nursling.—Neuweiler and Hubscher investigate whether pregnancy and lactation produce changes in the metabolism of ascorbic acid. First they give their attention to the problem as to how the fetal organism obtains the ascorbic acid necessary for its growth. They consider it demonstrated that the fetus receives the vitamin C from the maternal organism, for a synthesis of ascorbic acid in the fetal organism is highly improbable. The great ascorbic acid content of the placenta is a reserve placed by the maternal organism at the disposal of the fetus. Studies revealed that the blood of pregnant women has a much lower vitamin C content than has the blood of nonpregnant women. Tests on the urines of pregnant and lactating women disclosed that the vitamin C deficit is greatest in the nursing mothers. The authors also investigated the vitamin C content of the milk. They studied human milk, cow's milk and goat's milk, these being the only types of milk customarily used for the feeding of infants. They found that human milk contains from five to six times more vitamin C than does cow's or goat's milk. The animal species which are capable of effecting a synthesis of vitamin C have a milk that is poor in vitamin C. The quantity of vitamin C contained in the milk of women suffices for the normal needs of the infant, whereas the milk of cows and goats is insufficient in this respect. Comparative studies on the urinary elimination of vitamin C in nurslings revealed that infants receiving large amounts of vitamin C eliminate much more than those receiving little. It was found also that the quantity required by the nursling is relatively large; it amounts to approximately 6 mg. per kilogram daily. On the basis of their observations, the authors conclude that artificially fed infants must be given added quantities of vitamin C in the form of lemon juice or of a synthetic vitamin C product. Regarding the nursing mothers, they say that a rational diet furnishes nearly all the vitamin C necessary. One or two oranges a day suffice and more than cover the needs of the nursing mother.

Revue Neurologique, Paris

1: 329-448 (April) 1938

*Serous Meningitis. M. Molhant.—p. 329.

New Anatomoclinical Observation of Sclerosis with Acute Plaques. Riser and Geraud.—p. 348.

Serous Meningitis.—Molhant says that the term serous meningitis was employed first by Quincke to characterize the excessive production of cerebrospinal fluid with accumulation in the cerebrospinal spaces. Before taking up the different forms of serous meningitis, the author discusses the biologic physiology of the cerebrospinal fluid. He emphasizes the importance of the biologic equilibrium of the cerebrospinal fluid on the stimulation of the hypothalamic sympathetic centers and the role of the cerebrospinal fluid in the regulatory mechanisms of the humors. He shows that the clinical aspects of localized serous meningitis, at least in its simple forms, are the manifestation of an organofunctional pathogenic complex. The meningeal cyst is a sequel of a subacute inflammation of the brain and meninges. The treatment of choice is the intradermal tuberculin desensitization. Discussing the generalized cerebral serous meningitis, he takes up first the purely toxic forms, which are caused essentially by the noxious action of certain endogenic toxic substances. Hypertonic solutions of dextrose in massive doses, repeated for several days, have a remarkable curative action in the acute cases. The second type of generalized meningitis discussed by the author is the form that is due to toxic sensitization either by a medicinal or by an infectious factor. The reported histories indicate intoxication with phenobarbital, alcohol, gold salts and so on, the presence of chronic evolutive tuberculous processes or the combination of these medicinal and infectious factors. In these cases the administration of hypertonic solutions of dextrose constitutes the treatment of choice during the acute periods. In the chronic forms repeated lumbar punctures, decompressive craniectomy and other intracerebral interventions have been recommended. Roentgen treatment has also been recommended because under its influence the production of cerebrospinal fluid is decreased. The author utilized with good success intradermal tuberculin desensitization. This treatment is simple, inoffensive and at the disposal of the general practitioner. By its para-allergic action it dynamizes and regulates the apparatus of disturbed biologic regulation of the dyscrasic organism. It has a desensitizing action. By its specific allergic action it contributes also to the cure of the tuberculous lesions.

Schweizerische medizinische Wochenschrift, Basel

68: 443-528 (April 30) 1938. Partial Index

Symptomatology of Gastrocolic Fistula. B. Breitner.—p. 443.

Wire Extension. M. Kirschner.—p. 444.

Ablation of First Lumbar Ganglion in Painful Sequels of Phlebitis of Inferior Member. R. Leriche.—p. 451.

Rare Case of Cerebral Prolapse into Sinus Frontalis. O. Uffreduzzi.—p. 456.

*Return to Billroth I in Secondary Gastric Operations. P. Clairmont.—p. 461.

Abdominoperineal Amputation of Rectum. P. Decker.—p. 463.

Billroth I in Secondary Gastric Operations.—Clairmont points out that it was von Haberer who, by changing and improving the technic of Billroth's first method, made it suitable not only for the primary resection on account of gastric or duodenal ulcer but also for the complicated after-operations on account of disturbances after gastro-enterostomy. The author describes the clinical histories of three patients and demonstrates that the resection according to the first method of Billroth is the best intervention in counteracting the unfavorable results of gastro-enterostomy and in reestablishing physiologic conditions. Clairmont admits that the surgeon who uses Billroth's first method rarely or not at all for gastric resection will hardly find the courage to use this method in the more complicated cases of second or third interventions. However, the three reported cases, as well as other reports in the literature, demonstrate that especially in these complicated cases the first method of Billroth produces excellent results, which are not obtainable with other methods.

Archivio di Ortopedia, Milan

53: 639-896 (Dec. 31) 1937

Bilateral Bifurcation of Feet and Its Surgical Therapy. R. Marziani.—p. 639.
Early Treatment of Obstetric Torticollis with Plaster Collar Cast with Shoulder. R. Marziani.—p. 651.
Personal Technic in Treatment of Fractures of Clavicle and Its Results. R. Marziani.—p. 659.
Congenital Luxation of Hip Joint and Blood Group. E. Tranquilli-Leali.—p. 681.
*Etiology of Articular Osteochondroma. S. L. Carnevali.—p. 713.
Early and Late Congenital Osteogenesis Imperfecta: Analogies and Differentiation. A. Mastromarino.—p. 729.
Clinical Semeiology of Lameness. P. Antonio.—p. 805.

Etiology of Articular Osteochondroma.—Carnevali made microscopic studies of osteochondromatous nodules which had been removed surgically from the knee of a patient. The patient, aged 40, had had gonorrheal purulent arthritis, which was treated by arthrotomy. Some years later roentgen examination of the knee joint showed intra-articular calcification. On operation a great number of nodules, both loose and adherent to the synovial membrane, were found and removed. On microscopic study the loose nodules were found to be in the final stage of a proliferating process. The cartilage was preserved by osmotic nutrition. The osteogenic process was still in progress in the center of the pedunculated nodules, while the cartilaginous layer was well preserved. The author reviews the literature and discusses the infectious, traumatic and embryologic theories on the pathogenesis of intra-articular osteochondroma. He believes that the disease is due to the presence of intra-articular infection or of acute or chronic inflammation which induces alterations of the physicochemical condition of the synovial membrane with consequent primary hyperplasia and secondary metaplasia. The metaplasic synovial villi develop into the chondromatous nodules, in the center of which processes of calcification and ossification take place as long as the nodules have vascular connections with the synovial membrane (sessile and pedunculated nodules). When the nodules become detached from the synovial membranes, the phenomena of calcification and ossification of the center of the nodules stop. The bone portion of the nodules appears as atrophic old bone, whereas the cartilaginous layer of the nodule shows a living aspect since it continues to receive nutrition by osmosis.

Studium, Naples

28: 97-120 (May 1) 1938

Treatment of Ancylostomiasis. M. Mazzitelli.—p. 97.
*Secretory Functions of Stomach in Course of Atropa Belladonna Treatment. E. Nicolini.—p. 99.

Stomach During Treatment with Belladonna.—Nicolini determined the secretion of hydrochloric acid in the stomach in two groups of patients who had postencephalitic parkinsonism and who were being treated with atropa belladonna. In one group of fifteen patients the treatment had been given for a short time in small doses. In the other group of sixteen patients it had been given for a long time in large doses. Determinations of the hydrochloric acid secretion were made by examination of the gastric secretion, which was withdrawn at intervals of fifteen minutes during the first hour after administration of an Ewald meal test. The author found that in the majority of cases the hydrochloric acid secretion is diminished before the treatment is given, in the course of which it diminishes still more. In a few instances achlorhydria appears. There is no fixed therapeutic dose by which lasting inhibition of the hydrochloric acid secretion may be induced, as the effect depends on the individual tolerance and ability of the patient to accustom himself to the drug. Small doses of belladonna may inhibit the hydrochloric acid secretion in some cases, whereas large doses are necessary to inhibit it in others. In some cases in which the secretion is normal before the treatment, it does not change in the course of the treatment, even though paralysis from the vagus develops in other parts outside the gastric territory. In some patients showing hyperchlorhydria before the treatment, the hydrochloric acid secretion becomes normal in the course of the treatment. According to the author the results of his observations show that the secretory functions of the stomach do not depend entirely on vagal innervation. The latter conception should be kept in mind when the production of lasting changes of the gastric secretion, by means of vagal inhibition, is indicated in the treatment of certain diseases, such as in the treatment of hypersecretory neurosis by atropine.

Hospital, Rio de Janeiro

13: 751-956 (May) 1938. Partial Index

Tests for Function of Liver and Biliary Tract. J. Vilela Pedras.—p. 783.
Lobitis of Azygos Lobe: Case. A. L. Stockler.—p. 817.
Cervicothoracic Sympathectomy in Treatment of Paroxysmal Respiratory Syndromes. M. C. de Mota Maia.—p. 823.
Thalamencephalic-Hypophysial Adiposity (Adiposis and Underdevelopment of Genitalia, Frölich's Type). Monteiro de Carvalho.—p. 857.
Pyloric Spasm: Case. M. Vaz de Melo.—p. 891.
*Pleural Incontinence. A. Cordeiro Junior and F. Benedetti.—p. 913.

Pleural Incontinence.—Cordeiro Junior and Benedetti report two cases of incontinence of the pleura to pneumothoracic insufflations in patients with pulmonary tuberculosis. The insufflations of 200, 500 and 800 cc. of gas, in three different attempts, failed in each case to induce pneumothorax. There was no technical error. Roentgenoscopy showed no gas collection in the pleura. The roentgenograms showed no collapse of the lungs. According to the author, the cause of the refractivity of the pleura for pneumothorax is the presence of a pleurobronchial fistula without any spontaneous pneumothorax. The gas enters by the pleura and is immediately eliminated through the bronchi. Two factors are of importance: the presence of adhesions around the fistula, which prevent the formation of spontaneous pneumothorax (anatomic factor), and the expansion of the lung from stimulation of the vagus nerve (physiologic factor).

Klinische Monatsbl. f. Augenheilkunde, Stuttgart

100: 497-656 (April) 1938. Partial Index

*Ophthalmologic Studies on Uniovular Twins of Advanced Age: Hereditary Nature of Signs of Aging Process. A. Vogt.—p. 497.
Blood Pressure and Ocular Tension: Contribution to Pathology of Tabetic Atrophy of Optic Nerve. K. Albrich and F. Kukán.—p. 545.
Oligodendroglioma as Example of Primary Intradural Tumors of Optic Nerve. E. Schreck.—p. 560.
Glioblastic and Spongioblastic Genesis of Retinal Tumors. G. Favaloro.—p. 577.

Ophthalmologic Studies on Hereditary Nature of Aging.—Vogt points out that the various signs of senility in uniovular twins have such a degree of similarity or even identity that the formerly accepted opinions of the aging process as a result of environmental factors must be abandoned. The study of senile uniovular twins demonstrates that the signs of the process of aging are inherent in the germ plasm (uniovularity presupposes identical germ plasm of the twins) and that they appear with absolute uniformity at a certain age and in a predestined form. The author's conclusions regarding the hereditary character of the process of aging are based on observations on thirty-four sets of uniovular twins between the ages of 55 and 81. In this report he observes the symptoms of aging on certain parts of the eyes of uniovular twins. Discussing the senile changes on the conjunctiva, he shows that in aged uniovular twins pinguecula as well as spontaneous pterygium appear at about the same time and in the same localization, and he concludes that hereditary factors must play a part in the development of those defects. He further describes and illustrates senile changes on the cornea of sets of uniovular twins. He shows that unilateral, excessive atypical, premature, slight or absent arcus senilis must be hereditary, having observed identical characteristics not only in successive generations but also in sets of senile uniovular twins. Then he demonstrates the hereditary character of Krukenberg's pigment spindle and of the cornea guttata senilis. Following a discussion of the senile degeneration of the pigmented edge of the pupil and the hereditary predestination of this symptom, the author takes up the study of senile cataract in uniovular twins. That the type of senile cataract is hereditary he demonstrates on different sets of senile uniovular twins. Finally he shows that the senile changes in the vitreous body and in the fundus oculi of twins indicate the hereditary nature of these changes also.

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Zeitschrift für Immunitätsforschung, Jena

92: 281-444 (March 22) 1938. Partial Index

Experiments on Serologic Behavior of Native and Heated Blood Serum in Complement Fixation. E. Schwab.—p. 289.
Behavior of Bacterium of Scleroma and of His Dissociation Forms in Serum of Patient. W. Kuryłowicz and E. Mikulaszek.—p. 304.
Action of Heterogenic Protein Bodies. L. Kostyál.—p. 318.
Exotoxins and Endotoxins of Dysentery Bacilli: II. Further Studies on Endotoxins of Shiga and Flexner Dysentery Bacilli. R. Haas.—p. 355.
Epidemiologic Observations in Human Brucellosis in Japan and in Manchukuo. H. Hiroki.—p. 382.
*Adsorption of Virus of Foot and Mouth Disease by Aluminum Hydroxide with Especial Consideration of Immunizing Characteristics of Virus Adsorbents. S. Schmidt.—p. 392.

Adsorption of Virus by Aluminum Hydroxide.—Schmidt describes the development of an aluminum hydroxide preparation which has a strong adsorbent action for toxin and virus, particularly the virus of foot and mouth disease. The adsorption was studied on the virus in virulent lymph, in the extract from the aphthae, in the virulent serum and on the cultured virus. Virus adsorbents that are produced according to the author's technic are infectious for guinea pigs in case of intramuscular, intraperitoneal or intracutaneous injection. However, if introduced into the subcutaneous tissues the adsorbents are comparatively harmless but develop a rather potent and prolonged specific immunity against foot and mouth disease. It is possible to produce virus adsorbents that contain two or three types of viruses. A single injection of a preparation of this type may produce, under favorable conditions, a potent and permanent immunity against two or three types of viruses. Storage reduces the pathogenic characteristics of the virus adsorbents produced with aluminum hydroxide, but they retain, at least partly, the immunizing capacity. In case of comparatively high temperature, about 37 C., the rapid disappearance of the infectiousness is accompanied by a considerable reduction of the antigenic property. Freezing and drying destroy the pathogenic as well as the antigenic properties of the adsorbents. In the animal organism (subcutaneous tissue) the virus adsorbents undergo rapid changes. The pathogenic capacity disappears rapidly. However, the immunizing capacity is partly preserved and may still be demonstrated in adsorbents that have been in the animal organism for two weeks, in spite of the fact that the organism is already immune.

Zeitschrift für Kinderheilkunde, Berlin

59: 543-667 (April 2) 1938. Partial Index

*Intoxications by Ustilago Maydis (Ustilaginism) in Children. E. Mayerhofer and B. Dragišić.—p. 543.
Ascorbic Acid in Treatment of Nutritional Disturbances in Nurslings. Elisabeth Urbanitzky.—p. 553.
Sinus Thrombosis as Result of Trauma During Birth. A. Meier.—p. 556.
Experimental Investigations on Diphtheria of Mucous Membranes in Animals: Therapeutic Efficacy of Ordinary ("Native") and Purified and Concentrated Diphtheria Serum. F. von Bormann and Hildegard Ditton.—p. 559.
Inverse Anaphylaxis in Human Subjects: Contribution to Problem of Manifestations of Hypersensitivity in Human Subjects. E. A. Voss.—p. 612.
Behavior of Carbohydrate Tolerance of Diabetic Children in Various Types of Diets. H. Hungerland.—p. 649.

Ustilaginism in Children.—Mayerhofer and Dragišić describe observations on fifteen children with ustilaginism, but they also induced ustilaginism in mice and compared the symptoms in the animals with those in the children. They found that young children and nurslings are especially susceptible to ustilaginism and the animal experiments disclosed that young mice too are more readily poisoned with Ustilago maydis (smut of maize) than are older mice. Discussing the symptomatology of ustilaginism, the authors say that the disorder frequently begins with gastrointestinal disturbances in the form of diarrhea. Acropathic cutaneous manifestations, particularly severe burning, itching or formication on the palmar and plantar surfaces, is another important symptom. Hyperemia of the extremities often alternates with acrocyanosis. The alternating changes between hyperemia, cyanosis and pallor are noticeable also on the tip of the nose. It is suggested that this variable symptom is the result of an intoxication of the small cutaneous vessels and that the cutaneous edema of the arms and legs, which occurs in severe cases, is likewise a result of this impairment of the cutaneous vessels. If the acrocyanosis persists for longer periods, acrogangrene may develop. The authors observed this in three of the fifteen cases. On the mucous membranes, gums, lips, conjunctiva and so on, ustilaginism often elicits reddishness, swelling and itching. The tachycardia with hypertension which develops in the severe cases is one of the most persisting symptoms. Nervous disturbances are also likely to develop in cases of ustilaginism; there may be latent or manifest spasmophilia, muscular spasms and pains, nervous irritability, restlessness and delirium. Then there may be some nonessential secondary symptoms such as interdigital rhagades, pigmentations on the tips of the fingers and toes, sensitivity to sunlight and so on. Regarding the differential diagnosis, the authors say that if the anamnesis of a child with acropathy discloses that it has been fed with maize flour in which spores of Ustilago maydis can be seen the disorder may be diagnosed as ustilaginism rather than as true infantile acrodynia, ergotism or pellagra. Moreover, ustilaginism, even severe cases, usually responds to dietetic treatment within a few weeks, whereas acrodynia and pellagra last much longer.

Zeitschrift für klinische Medizin, Berlin

134: 1-128 (April 14) 1938. Partial Index

*Diagnosis of Addison's Disease from Blood Serum. O. Riml.—p. 1.
Treatment of Addison's Disease and Its Results. E. H. Rynearson, A. M. Snell and E. Hausner.—p. 11.
Views into Carbohydrate Metabolism by Study of Glycogenosis. F. Erben.—p. 31.
Therapy of Round Gastric and Duodenal Ulcer. J. Faltitschek and A. Wald.—p. 71.
Qualitative Thrombocytic Aspects in Agranulocytosis. J. Arneth.—p. 87.
*Pernicious Anemia in Course of Chronic Polyarthritis. A. Schneiderbaur.—p. 113.

Diagnosis of Addison's Disease from Blood.—In studies on changes in the composition of the blood of nephrectomized rabbits Riml found a substance which, when transferred to normal guinea pigs, produces signs of fatigue as well as changes in the adrenals that must be regarded as signs of an increased functional load, for they fail to develop when adrenal cortex extract is administered. The author decided to investigate whether changes similar to those in nephrectomized animals could be observed in patients with adrenal insufficiency. A dialysate of the serum of patients with Addison's disease was administered by intraperitoneal injections to guinea pigs. Control animals of the same size were given injections of a serum dialysate of persons without adrenal defects. Later the animals were killed and their adrenals subjected to microscopic examination. The author made the tests on three patients with Addison's disease. He found that the serum dialysate of these patients contains a substance which, when transferred to guinea pigs, produces in the adrenals of these animals changes which are interpreted as signs of an increased functional load. The severity of the changes in the adrenals of the test animals goes almost parallel with the severity of the Addison's disease in the patient. After the treatment with adrenal cortex extract the serum of the patient no longer contains the substance that causes changes in the adrenals of guinea pigs, but when the treatment with adrenal cortex extract is discontinued the substance reappears.

Pernicious Anemia in Chronic Polyarthritis.—Schneiderbaur describes three cases of primary chronic deforming polyarthritis in which, after this disorder had existed for several years, there developed a genuine pernicious anemia with all objective clinical and hematologic signs. In one of the cases the pernicious anemia developed immediately after an acute exacerbation of the articular disturbance. A causal connection between these disorders, which seems probable in view of the clinical symptomatology, seems even more likely on the basis of Castle's observations. It is suggested that the chronic polyarthritis, as an infectious process, produced by way of the hematogenic route a chronic gastritis with atrophy of the gastric mucosa and subsequent impairment of the secretory functions, so that in addition to the gastric achylia there was a cessation of the production of the intrinsic factor of Castle. This disturbance resulted in the development of a secondary pernicious anemia. The author's observations indicate that the infectious toxic factor is one of the causes that may lead to a cessation of the secretion of Castle's principle. He thinks that Naegeli's opinion that there are only three eliciting factors (syphilis, pregnancy and bothriocephalus latus) for secondary pernicious anemia is no longer tenable.

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Zeitschrift für Krebsforschung, Berlin

47: 209-302 (April 22) 1938

Experimental Investigation of Question of Pulmonary Cancer of Schneeberg Type. H. R. Döhnert.—p. 209.
Significance of Proteins for Processes in Pathogenesis of Cancer. R. Reding.—p. 240.
*Multiple Appearance of Tumors and of Tissue Deformities. I. Holmqvist and A. Nelson.—p. 257.
Improved Method of Vaccination in Research on Cancer. S. Konsuloff. —p. 273.
Clinical Considerations on Question of Occupational Cancer in Asbestos Workers. F. Hornig.—p. 281.
Occupational Cancer in Asbestos Workers. M. Nordmann.—p. 288.

Multiple Appearance of Tumors.—Holmqvist and Nelson state that a number of investigators have given their attention to the exact definition of the term primary multiplicity but have failed to agree. However, all of them emphasize how important and difficult it is to differentiate metastases from the primary multiple tumors. The authors aim to show under what conditions multiplicity occurs and what factors influence multiplicity and to compare the results obtained on their own material with those obtained by other authors. For this reason their method of classification was to a certain extent influenced by that of others. Like Puhr, the authors have classified hypertrophy of the prostate with the tumors, although they are aware that the blastomatous nature of this hypertrophy may be questioned. The material on which the authors base their conclusions comprises 4,000 unselected cases that came to necropsy at the hospital of St. Erik in Stockholm. Tumors were discovered in 55.8 per cent of the cases. Primary multiplicity of tumors was discovered in 22.5 per cent of the cases. The multiplicity seems to be influenced by age and sex. A tendency to multiple appearance seems to increase with the years; women have a greater tendency for multiplicity than have the men of the same age. Multiplicity is more frequent in benign than in malignant tumors. The following combinations are especially frequent: uterine myomas and uterine polyps, benign tumors of the uterus and benign tumor of the endocrine organs, particularly of the thyroid, and finally benign tumors in the different portions of the digestive tract. A tendency for the formation of benign tumors may involve the entire body, a system of organs, organs or parts of organs. Factors prevailing in case of primary multiplicity of tumors justify the assumption of a probably genetically conditioned local diathesis. Moreover, the authors suggest the possible existence of a similar generalized tumor diathesis.

Wiener medizinische Wochenschrift, Vienna

88: 425-452 (April 16) 1938. Partial Index

Anomalies in Soft Sections of Birth Channel and Their Treatment. L. Kraul.—p. 426.
*The Lungs as Most Frequent Seat of Primary Foci of Rheumatic Infection. J. Havas.—p. 440.
Vitamin B_2 (Riboflavine) Treatment. S. Kalter.—p. 446.

Lungs as Foci of Rheumatic Infection.—On the basis of four case records, Havas says that the possibility of primary pulmonary foci of rheumatic infection is established. The high statistical incidence of chronic bronchitis among rheumatic patients in whom no other demonstrable foci, such as teeth or tonsils, exist indicates that the majority of rheumatic disorders are of pulmonary origin. The rheumatic foci are based on pulmonary lesions of the ulcerous-cavernous type which have healed by scarring. Rheumatic alterations and lesions in the joints and their adnexa depend on local allergic influences, which are released in some instances by the bacilli of tuberculosis but most frequently by the common bacteria of the mixed infection of ulcerous pulmonary processes.

Polska Gazeta Lekarska, Lwów

17: 353-376 (May 1) 1938

Structural Alterations of Aorta in Children and Their Relation to Sclerosis. Z. Albert.—p. 353.
The Problem of Negative T_3. B. Tanne.—p. 357.
*Roentgen Therapy of Malignant Granuloma. M. Spritzer.—p. 360.
Comparative Research on Rheumatic Reactions. E. Bokser and J. Szubarga.—p. 363.
Experimental Research and Clinical Action on Digitalis (Gitolan). J. Walawski and H. Rasolt.—p. 365.

Roentgen Therapy of Malignant Granuloma.—Spritzer has treated fifty-six patients with malignant granuloma by roentgen therapy. He divided them into two groups. In group 1 twenty-seven patients had been treated between the years 1926 and 1932. These patients had been given low voltage roentgen therapy averaging from 200 to 300 skin doses in the region of the external glands and from 500 to 600 skin doses in the region of the internal glands. This series of roentgen therapy was repeated after several months had elapsed, according to the physical condition of the patient. In group 2 there were twenty-nine patients to whom roentgen therapy had been applied between the years 1932 and 1936. These patients had been given large fractional doses, externally from 800 to 1,200 roentgens and internally as much as 5,000 roentgens. In cases of relapse, roentgen therapy was repeated. It has never been applied on healthy glands. In conclusion he says that roentgen therapy of malignant granuloma cannot be employed schematically but must be used individually. It should be applied only to diseased glands, the rest of the lymphatic system being spared as much as possible. It should be administered only in case of relapse and not as a preventive. In the early stages of disease weak doses should be prolonged, if possible, in order to lengthen the life of the patient. In later stages it is necessary to give more intensive treatment. Roentgen therapy should be applied also to the bones in each case.

Medichniy Zhurnal, Kiev

7: 1117-1551 (No. 4) 1938. Partial Index

Second International Congress on Blood Transfusion (Paris). O. O. Bogomolets.—p. 1127.
Pathogenesis of Grave Posttransfusional Reactions not Dependent on Blood Groups. O. O. Bogomolets.—p. 1137.
Albumin Content of Tissues in Experimental Hyperproteinization and Hypoproteinization. N. B. Medvedeva.—p. 1145.
Supravital Staining of Surviving Sections of Normal Tissues in Physiologic and Hypotonic Surroundings. E. Smoilovskaya.—p. 1354.
*Genesis of Cerebral Gliomas. V. G. Lazarev and A. D. Dinaburg.—p. 1369.

Genesis of Brain Gliomas.—Lazarev and Dinaburg studied eighty instances of glioma and found that 25 per cent of them exhibited embryonic origin. Considered from an embryologic point of view, the tumors were divided into four groups: (1) those of dystrophic origin, (2) those exhibiting embryonal foci enabling one to follow the course of development of the growth, (3) those associated with anomalies and developmental malformations and (4) those in which glioma was associated with gliomatosis. The first group was represented by seven cases, of which six were in children, with a localization in the region of the vermis of the cerebellum, tumors of the median line designated cytologically as medulloblastomas. The development of these tumors in children, their median localization corresponding to the fissure in the closure of the neural tube—regions giving rise to a number of anomalies and developmental malformations—speaks in favor of embryonal origin. In three of these cases the authors found a hyperplasia of the reticular tissue and they felt justified in designating this variety of tumor a reticuloglioma. A second group, consisting of four astrocytomas, exhibited a conglomeration of cells identical with "growth centers" described by Obernsdorfer in ganglioneuromas and neurinomas. These growth centers were localized principally in the neighborhood of blood vessels. In some instances they consisted exclusively of elements characteristic of an early embryonal stage (medulloblasts); in others there were found, in addition, more mature types of cells representing a transition to astrocytes. As a rule, mature astrocytes are found outside the growth centers. The transitional elements may be found scattered throughout the tumor tissue. In one case of astrocytoma there was observed along with the growth centers an additional tumor consisting of embryonal elements. The presence of a second mature astrocytoma in the opposite hemisphere of the brain enables one to regard growth centers as a manifestation of multicentral growth of the tumor. The third group was represented by three cases in which glioma was associated with heterotopias, irregular formation of the radiations of the cerebellum, development of accessory radiations, and so on. The fourth group was represented by seven cases in which, in addition to the circumscribed growth of the type of astrocytoma, there was observed in the opposite hemisphere gliomatous proliferation representing a developmental anomaly of glial tissue capable of transformation into a genuine glioma under conditions that are still not understood.

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Nederlandsch Tijdschrift v. Geneeskunde, Amsterdam

82: 1683-1806 (April 9) 1938. Partial Index

New Electrocardiographic Aspects of Angina Pectoris. C. L. C. Van Nieuwenhuizen, H. A. P. Hartog and E. Matthijssen.—p. 1695.
Exophthalmos in Hyperthyroidism. L. P. Daniels.—p. 1704.
*Flavadine Treatment in Gonorrhea of Women. R. Simons and C. A. Eindhoven.—p. 1713.
Severe Nicotine Poisoning by Nicotine Gas. H. N. Kemme.—p. 1718.

Gonorrhea in Women.—Simons and Eindhoven report their experiences with an acridine derivative in the treatment of eighteen women with gonorrhea. The preparation used by the authors was flavadine, an acridine preparation which contains arsenic in an organic combination and which, while not irritating like acridine hydrochloride, nevertheless has a good gonococcidal action. The preparation was first used for the treatment of gonorrhea in 1932. Favorable reports about the preparation induced the authors to employ it in acute cases of gonorrhea, in preference to the new sulfanilamide preparation, which is better suited for the chronic cases. Before treatment is instituted, cultures are made from material obtained from the urethra, cervix and rectum. In the treatment of the cervix uteri, the organ is exposed with the aid of a speculum, the secretion is wiped away and then the flavadine is introduced by means of a syringe. At first 1 cc. is administered, then 2 cc. and then 3 cc. If some of the fluid flows back, it is wiped away to avoid erosions. For greater safety a tampon is introduced into the vagina; this can be removed by the patient on the following morning. The treatments are given daily for eight days. After each series a control test is made. From one to six series are required for the treatment of cervical gonorrhea, but the average is about three series of eight days each. In approximately half of the women treated, the cervix was cured after eight days. In rectal gonorrhea, in which flavadine was equally effective, 5 cc. was instilled and from one to four series of treatments were required for cure. The urethra was not treated with flavadine but rather with the usual silver preparations. The silver therapy required one or two months longer than the treatment with flavadine, but the cervix was never reinfected from the urethra. Reviewing the results of the flavadine treatment, the authors say that all eighteen women were cured. Control examinations extending over periods of from three to twelve months proved that there was only one relapse, which actually may have been a reinfection. On the basis of these observations the authors think that flavadine is the remedy of choice in the local treatment of gonorrhea in women.

82: 1807-1894 (April 16) 1938

Blue Fluorescence of Urine in Ultraviolet Light Caused by Indoxyl Compounds. G. A. Kreuzwendedich von dem Borne.—p. 1808.
Apparatus for Measurement of Mean Diameter of Erythrocytes. L. Schalm.—p. 1817.
*Ureteronephrectomy in Treatment of Renal Tuberculosis. C. Van Gelderen.—p. 1820.
Thrombosis in Puerperal Women. D. G. Wesselink.—p. 1831.
Acute Intestinal Invagination in Nurslings and Early Diagnosis. L. D. J. Thorbecke.—p. 1834.

Ureteronephrectomy in Renal Tuberculosis.—Van Gelderen reports that in a series of thirty-seven patients with renal tuberculosis primary ureteronephrectomy was carried out systematically. This did not augment the risk for the patient, in the form either of an increased operative mortality or of a higher mortality shortly after operation. The ureteral wound nearly always healed primarily and permanently; disturbance in the healing of the renal wound did not occur less frequently than in simple nephrectomy, so that the ureter cannot be looked on as the cause of this disturbance, except in rare cases of long standing. Ureteral empyema, cold abscess and acute abdominal pains are prevented. Even in the unfavorable class of patients the lasting results were found to be favorable; only three patients died, and in all the mortality was of the remote type. Thus nothing was experienced of the disadvantages ascribed to the method by some; the expected advantages to some extent were not found (wound healing), but if present they could clearly or most probably be ascribed to the ureteronephrectomy (lasting results, rapid healing of the bladder). The operation deserves to be advocated.

Acta Medica Scandinavica, Stockholm

95: 129-436 (April 29) 1938. Partial Index

Source of Error in White Blood Count. J. Engelbreth-Holm and C. C. Winkel Smith.—p. 129.
Hemorrhagic Thrombocythemia. U. Uotila.—p. 136.
*Physiologic Mechanism of Decrease of Acidity in Gastric Contents. W. N. Boldyreff and W. F. Martin.—p. 151.
Studies on Hemoglobinuria. F. L. J. Jordan.—p. 319.
Studies on Urinary Sediment: I. Technic. A. Næraa.—p. 341.
*Id.: III. Effect of High Protein Diet on Course of Nephritis, with Special Reference to Urinary Sediment. A. Næraa.—p. 359.
*Id.: IV. Urinary Sediment in Men Riding a Six Day Bicycle Race. A. Nærra.—p. 383.

Mechanism of Decrease of Acidity in Gastric Contents.—Boldyreff and Martin maintain that the chief factor in limiting the acidity of the gastric contents is food, particularly protein, but they do not discuss this phase of the problem. They emphasize that there is no such thing as hyperacidity, because gastric juice is always secreted with a definite degree of acidity of about 0.5 per cent of hydrochloric acid. They think that it would be better to abandon the term hyperacidity, substituting for it a more fitting term such as hypersecretion. Discussing the disagreement between clinicians and physiologists about the acidity of gastric juice, they say that for about 100 years clinicians considered it to be about 0.15 per cent, whereas the physiologists since the time of Heidenhain have maintained that it was about 0.5 per cent. Only in the twentieth century did the investigation of so-called duodenal regurgitation furnish an explanation. The authors describe the phenomenon of regurgitation of the duodenal contents into the stomach containing acid. They describe and discuss experiments by Boldyreff, Lewis and Slagle. The tests that were made on man and dogs may be classed in three groups: The first group demonstrates that in the presence of acids in the stomach there always is a decrease in the acidity (neutralization of acidity). Analyses of the chloride content, after hydrochloric acid has been administered, indicate that the main part is played not by dilution of the liquid but by binding of the acid. The second group of experiments demonstrates that neutralization is effected from the duodenum, because, if the stomach or a portion of it is isolated, the neutralization is never normal. The presence of bile and intestinal mucus during the process of neutralization explains the source of the liquid which binds the acid. The third group of experiments shows that removal of duodenal fluids almost entirely excludes the process of neutralization. The authors reach the conclusion that the main factor in the neutralization of acidity in the stomach is the alkaline pancreatic juice which is regurgitated from the duodenum while there is still powerful acid present in the stomach. The gastric mucus also effects a certain binding of the acid introduced into the stomach. Dilution plays an insignificant part in the reduction of the acidity of the gastric contents. Normally this is achieved by the pancreatic juice which comes from the intestine. In pathologic cases, with insufficient action of the pancreatic gland, dilution is achieved by saliva, bile and intestinal juice. Participation of the pyloric juice is also quite probable.

High Protein Diet in Nephritis.—It is pointed out by Næraa that, owing to the complete failure of drug therapy in hemorrhagic nephritis, the diet has always been an important problem in the treatment of this disease. A milk diet was long considered preferable. In recent years, however, it has been replaced by a diet rich in carbohydrate but poor in protein. Ever since 1879, when Aufrecht set up his strict diet, protein has practically been banned from the diet of nephritic patients. In the last six or seven years, various authors (encouraged in particular by Epstein's studies on the pathology of nephrosis) have insisted more and more convincingly that protein ought to be introduced in the treatment of nephritis. In 1925 Addis gave a method for the determination of the numbers of erythrocytes, leukocytes, epithelial cells and casts in the urine. In 1933 the author adopted this method in order to study the possible noxious effect of a high protein diet on patients with acute nephritis. The plan was to give patients with acute or latent hemorrhagic nephritis alternatingly low and high protein diets. As soon as the patients entered the hospital they were put on a diet consisting of 250 Gm. of cream, 250 Gm. of milk, 250 Gm. of fruit, 200 Gm. of bread, 500 Gm. of green vegetables, 100 Gm. of potatoes, 100 Gm. of butter and 250 Gm. of oatmeal porridge

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with sugar. Only if the patients on admission were seriously ill, with oliguria, nausea and vomiting, were they given another diet, i. e., a limited supply of water and almost an absolute fasting diet. As soon as they had any desire for food they were given the aforementioned diet. This diet represents a daily intake of about 2,750 calories with a protein content of about 40 Gm. Each patient was kept on this diet for a variable length of time, while he was under observation and the diagnosis was established. The feature that decided when the patient was to be given the high protein diet was most often behavior of the hematuria. As a rule the author waited till the hematuria had become fairly constant as estimated by daily counts. The high protein diet consisted of the same food articles as previously listed, except that the 250 Gm. of oatmeal porridge was replaced by 250 Gm. of lean beef, usually in the form of a steak. Given in this way, the diet represents more than 3,000 calories and contains about 125 Gm. of protein. The patients were given these two diets alternately, through periods varying from eight to nineteen days. Quantitative examination of the urinary sediment in ten patients having various forms of hemorrhagic nephritis who were treated in this manner showed nothing to suggest that a high protein diet is injurious to the kidneys of such patients.

Urinary Sediment After Six Day Bicycle Race.—Næraa says that, since Addis in 1925 presented his method for quantitative urinary sediment determination and demonstrated the occurrence of hyaline casts and red blood cells in the urine of normal persons, the interest in the physiologic variations in the amount of these elements has been aroused anew. The fundamental question now arises whether physical exertion produces an increase in the number of erythrocytes and casts normally present in the urine and whether other kinds of casts besides the hyaline may appear under the same conditions. In order to elucidate this question the author made sediment counts on thirty-four specimens of urine from twelve men who took part in a six day bicycle race in Copenhagen in 1934. He used the method of Addis. He says that his studies on the urinary sediment of these men disclosed no signs of renal lesions.

Nordisk Medicin, Stockholm

95: 437-538 (May 13) 1938. Partial Index

Observations on Hypopituitarism: Contribution to Early Diagnosis. H. Zondek.—p. 437.
Fractional Analysis of Alveolar Air After Inspiration of Hydrogen as Method for Determination of Distribution of Inspired Air in the Lungs: Examinations of Normal Persons and of Patients Suffering from Bronchial Asthma and Pulmonary Emphysema. E. Roelsen.—p. 452.
*Occurrence of Different Types of Pneumococci in Cases of Acute Pneumonia in Stockholm. S. Gard, G. Löfström and G. Jacobsohn.—p. 483.
Etiology of Epidemic Hepatitis. T. T. Andersen and S. Tulinius.—p. 497.
Valve Stenosis of Main Bronchus. B. Söderling.—p. 510.

Types of Pneumococci in Acute Pneumonia.—Gard and his associates point out that the type differentiation of the pneumococci has opened up fresh avenues of approach for the study of the epidemiology and therapy of the pneumococcic infections. The satisfactory experiences gained abroad with specific serum therapy have led to its being tried in Sweden. The aim of the researches reported in this paper has been to ascertain the importance of various types of pneumococci as a cause of pneumonia. The authors reach the conclusion that the sharp line of distinction between croupous lobar pneumonia and catarrhal bronchopneumonia cannot be maintained. Acute pneumonia presents varying pathologico-anatomic appearances ranging from the fibrinous, lobar form, passing gradually into catarrhal bronchopneumonia and showing intermediary and mixed forms with variations in regard to the abundance of fibrin and the lobar dispersion. The pathologico-anatomic diagnosis made on the basis of clinical and roentgenologic observations is of course of value in determining the prognosis, but its importance in that respect is enhanced if it is supplemented by a bacteriologic investigation, which moreover is absolutely essential as a preliminary to a specific therapy. The authors have not been able to confirm Gundel's theory that the pathologico-anatomic aspect of pneumonia is determined entirely by the serologic type of the pneumococci. Other factors play at least as important a part in this respect. If, then, it is hardly justifiable from that point of view to ascribe any special position to types 1 and 2, nevertheless it cannot be denied that type 1 predominates in the frequency statistics in spite of the fact that several of the other types have proved to be capable of causing pneumonia with as high a rate of mortality or one even higher. Gundel's assumption that dissimilarities in the mechanism of infection (exogenous-autogenous infection) is the decisive factor in this respect can hardly be accepted as a satisfactory solution of the problem. From the investigations the authors have carried out it appears that approximately half of the lobar forms of pneumonia are caused by pneumococcus type 1, so that the production of type 1 serum for therapeutic use must be regarded as one of the most important means of reducing mortality from pneumonia. The next step would be to make serum against types 2 and 7. The experience gained abroad as to the effect of serum against these three types of pneumococci has been extremely favorable.

Hygiea, Stockholm

100: 177-224 (March 31) 1938

*Meningeal Hemorrhages, Originating from Rupture of Aneurysm in Basal Arteries of Brain. R. Luft.—p. 177.
*Gas Phlegmon in Lund Surgical Clinic from 1920 to 1936: Cases. F. Koch.—p. 194.

Meningeal Hemorrhages.—Luft reported twenty-five cases of meningeal hemorrhages due to rupture of an aneurysm in the basal arteries of the brain. The most frequent localization was the middle cerebral and the anterior communicating arteries. The aneurysms varied in size but were usually as large as a pea. He says that, on rupture of the aneurysm, intrameningeal hemorrhage along the base of the brain generally occurs. In many cases the hemorrhage in the meninges is complicated by disturbances in the brain parenchyma near the aneurysm. Lumbar puncture, done in eleven cases, showed microscopic blood in two and macroscopic mixture with blood in nine. The pressure of the spinal fluid was abnormally high. The combination of sudden cerebral symptoms and sudden stiffness of the neck supports the diagnosis of ruptured aneurysm. The smaller hemorrhages cause dulness and apathy; the more massive bleedings may result in death without the patient's return to consciousness (nine cases). Irritation of the brain cortex causes spasms, a common symptom. If the hemorrhage damages the brain substance near the aneurysm, hemiplegia and hemiparesis result (nine cases). In eleven cases there were disturbances in the pupillary reflex; in six, anisocoria; in five, paresis of the muscles of the eye; paralysis of the facialis nerve occurred in four cases, all with aneurysm in the anterior cerebral artery. The symptoms may suddenly disappear, to be followed by a second hemorrhage, often in a period free from symptoms. The blood pressure is frequently no higher than is normal for the patient's age. Atherosclerosis appeared in only two of the patients under the age of 60, and was no more marked in the patients over 60 than was to be expected at the age. The theory that atherosclerosis is the primary cause of the aneurysm or the immediate factor in cases of congenital defect in the wall of the blood vessel is therefore not accepted. There was neither history nor sign of syphilis in any case. Great importance is attached to congenital defects. While the author has found no record of any case in which there was recovery, in two reported cases the first hemorrhage occurred seventeen and twenty-one years, respectively, before the second, fatal hemorrhage (Fearnside).

Gas Phlegmon in Lund Surgical Clinic.—Six of Koch's twenty-four cases of gas phlegmon were fatal. Twenty-one were the result of accidents (nineteen complicated fractures, two lacerations of the soft parts). Gas phlegmon thus occurred in 3 per cent of the 700 cases of complicated fractures or more extensive lacerations of the soft parts in which treatment was given during the period from 1920 to 1936. All the accident patients were admitted within two and a half hours after the injury. In most cases the early symptoms of gas phlegmon appeared in from half a day to three days after the injury, in two cases in five and seven days respectively. The incubation period for the fatal cases was from one to seven days. Of the ten patients treated by amputation within six hours, nine recovered; of the nine in whom amputation was done after six hours of expectation, five recovered, and of the five treated conservatively, four recovered.

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This is an index to all the reading matter in THE JOURNAL. In the Current Medical Literature Department only the articles which have been abstracted are indexed.

The letters used to explain in which department the matter indexed appears are as follows: "BI," Bureau of Investigation; "E," Editorial; "C," Correspondence; "ab," abstracts; the star (*) indicates an original article in THE JOURNAL.

This is a subject index and one should, therefore, look for the subject word, with the following exceptions: "Book Notices," "Deaths," "Medicolegal Abstracts" and "Societies" are indexed under these titles at the end of the letters "B," "D," "M," and "S." State board examinations are entered under the general heading State Board Reports, and not under the names of the individual states. Matter pertaining to the Association is indexed under "American Medical Association." The name of the author, in brackets, follows the subject entry.

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For index to Organization Section see page 243B.

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Am.—American *Nat.—National*
A.—Association *Phar.—Pharmaceutical*
Coll.—College *Phys.—Physicians*
Conf.—Conference *Rev.—Revision*
Cong.—Congress *Ry.—Railway*
Conv.—Convention *Soc.—Society*
Dist.—District *Surg.—Surgery*
Hosp.—Hospital *Surgs.—Surgeons*
Internat.—International *S.—Surgical*
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